Chapter 9

Identification and Hazard Evaluation of Chemicals across the Hydraulic Fracturing Water Cycle

9. Identification and Hazard Evaluation of Chemicals across the Hydraulic Fracturing Water Cycle

9.1. Introduction

Chapters 4 through 8 of this assessment each present a stage of the hydraulic fracturing water cycle and the mechanisms by which activities in those stages produce potential impacts on drinking water resources. In contrast, this chapter presents and integrates what is known about chemicals *across* stages of the hydraulic fracturing water cycle (i.e., used in hydraulic fracturing fluids and detected in hydraulic fracturing wastewater). The discussion is focused on available information about (1) chronic toxicity values—specifically, the available noncancer oral reference values (RfVs) and cancer oral slope factors (OSFs)—of chemicals that could occur in drinking water resources; and (2) properties of chemicals that could affect their occurrence in drinking water resources (see Chapters 5 and 7).[1,2] To the extent that information was available to do so, knowledge of toxicological and chemical properties was combined to illustrate an approach that may provide preliminary insights about the relative hazard potential that chemicals could pose to drinking water resources.

Risk assessment and risk management decisions will be informed by the scientific information on the toxicity of chemicals in hydraulic fracturing fluid and wastewater, which recent authors note is incomplete (Goldstein et al., 2014). The U.S. House of Representatives' Committee on Energy and Commerce Minority Staff released a report in 2011 noting that more than 650 products (i.e., chemical mixtures) used in hydraulic fracturing contain 29 chemicals that are either known or possible human carcinogens or are currently regulated under the Safe Drinking Water Act (House of Representatives, 2011). However, that report did not characterize the potential toxicity of many of the other compounds known to occur in hydraulic fracturing fluids or wastewater. More recently, Kahrilas et al. (2015) reviewed the toxicity and physicochemical properties of biocides used in hydraulic fracturing. Stringfellow et al. (2014) examined the toxicity and physicochemical properties of several classes of chemicals that are reportedly used in hydraulic fracturing; however, this study only reported acute toxicity (from lethal doses), which may differ from the effects of low-dose, chronic exposure to these chemicals. Wattenberg et al. (In Press) assessed the acute and chronic toxicity data that was available for 168 chemicals from the FracFocus database that had at least 25 reports of use in North Dakota. The authors found that 113 of these chemicals had some health hazard data available, but determined that there were significant data gaps, particularly with regards to what is known about the potential chronic toxicity of these chemicals. Overall, available

[1] A reference value (RfV) is an estimate of an exposure for a given duration to the human population (including susceptible subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime. RfV is a generic term not specific to a given route of exposure. In the context of this chapter, the term RfV refers to reference values for noncancer effects occurring via the oral route of exposure and for chronic durations, except where noted. Source: IRIS Glossary (U.S. EPA, 2011d).
[2] An oral slope factor (OSF) is an upper-bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime oral exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per mg/kg day, is generally reserved for use in the low dose region of the dose response relationship, that is, for exposures corresponding to risks less than 1 in 100.

information indicates that there may be hundreds of chemicals associated with the hydraulic fracturing water cycle for which toxicological data is limited or unavailable.

Furthermore, the potential public health impact of hydraulic fracturing processes is not well understood (Finkel et al., 2013; Colborn et al., 2011). Potential public health implications are highlighted in the recent studies by McKenzie et al. (2014) and Kassotis et al. (2014), but as of early 2015, there is a lack of published, peer-reviewed epidemiological or toxicological studies that have examined health effects resulting from water contamination due to hydraulic fracturing. However, numerous authors have noted that with the recent increase in hydraulic fracturing operations there may be an increasing potential for significant public health and environmental impacts via ground and surface water contamination (Goldstein et al., 2014; Finkel et al., 2013; Korfmacher et al., 2013; Weinhold, 2012).

This chapter provides a compilation of the chemicals used or released during the fracturing process, and information about their potential health effects. The data are presented in this chapter as follows.

Section 9.2 discusses how ten information sources, including the EPA's analysis of the FracFocus database (U.S. EPA, 2015a), were used to create a list of chemicals used in or detected in various stages of the hydraulic fracturing water cycle. This chemical list was initially presented in the EPA's 2012 interim progress report (U.S. EPA, 2012f), and has been updated in this assessment with additional chemicals from FracFocus. The consolidated chemical list includes chemicals that are reportedly added to hydraulic fracturing fluids in the chemical mixing stage, as well as fracturing fluid chemicals, formation chemicals, or their reaction products that may be carried in flowback or produced water. Although over half of the chemicals cited on this list are listed in the EPA FracFocus database, this chapter is not meant to be interpreted as a hazard evaluation of the chemicals listed in the EPA FracFocus database alone.

Section 9.3 provides an overview of the methods that were used for gathering information on toxicity and physicochemical properties for all chemicals that were identified in Section 9.2, and outlines the number of chemicals that had available data on these properties. For toxicological data, the primary focus is on peer-reviewed, selected chronic oral RfVs and OSFs. This section also discusses additional potential sources of toxicity information: estimates of toxicity predicted using Quantitative Structure Activity Relationship (QSAR) modeling, or toxicological information available on the EPA's Aggregated Computational Toxicology Resource (ACToR) database. This chapter is focused on potential human health hazards of chemicals for the oral route of exposure (drinking water); therefore, the toxicological properties and physicochemical ranking metrics described herein (see below) do not necessarily apply to other routes of exposure, such as inhalation or dermal exposure. In addition, this analysis is focused on individual chemicals rather than mixtures of chemicals used as additives. Furthermore, the propensity for a chemical to pose a physical hazard (e.g. the flammability and explosiveness of stray gas methane) are not considered here.

Many chemicals reported in hydraulic fracturing were identified as being of interest in previous chapters of this report. This includes the most frequently used chemicals in hydraulic fracturing fluid (Chapter 5), the most and least mobile chemicals in hydraulic fracturing fluid (Chapter 5), and inorganic chemicals and pesticides that may be detected in flowback and produced water (Chapter 7). The available selected chronic oral RfVs and OSFs for these chemicals are summarized in Section 9.4.

Section 9.5 describes the hazard identification and hazard evaluation of chemicals for which data was available on toxicity, occurrence, and physicochemical properties.[1,2] For hazard identification, the selected chronic oral RfVs and OSFs and health effects for these chemicals are presented and summarized. To illustrate one approach to integrate toxicity, occurrence and physicochemical properties data to generate a hazard potential score, a multicriteria decision analysis (MCDA) framework was developed. In this context, occurrence and physicochemical property data were used as metrics to estimate the likelihood that a chemical could impact drinking water resources. Chemicals considered in these hazard evaluations include a subset of chemicals from the FracFocus database, as well as a subset of chemicals that have been detected in flowback and produced water.

In general, characterizing chemicals and their properties on a national scale is challenging and that the use and occurrence of chemicals is likely to differ between geological basins and possibly on a well-to-well basis (see Chapters 5 and 7). Therefore, for the protection of public health at the community level, chemical hazard evaluations may be most useful to conduct on a regional or site-specific scale. This level of analysis is outside the scope of this report; however, the methods of hazard evaluation presented here can also be applied on a regional or site-specific scale in order to identify chemicals that may present the greatest potential human health hazard.

9.2. Identification of Chemicals Associated with the Hydraulic Fracturing Water Cycle

As the initial step towards developing a hazard evaluation, the EPA compiled a list of chemicals that are used in or released by hydraulic fracturing operations across the country (U.S. EPA, 2012f). Ten sources of information (described in Appendix A) were used to develop this list. This consolidated list was used to compile two sublists: (1) a list of chemicals known to be used in hydraulic fracturing fluids, and (2) a list of chemicals that are reported to have been detected in hydraulic fracturing flowback and produced water. It is likely that, as industry practices change, chemicals may be used or detected that are not included on these lists. In addition, those chemicals that are considered proprietary and identified as confidential business information (CBI) by well operators are not listed or considered.

[1] Hazard identification is a process for determining if a chemical or a microbe can cause adverse health effects in humans and what those effects might be. See Terms of Environment at: http://iaspub.epa.gov/sor_internet/registry/termreg/searchandretrieve/termsandacronyms/search.do.

[2] Hazard evaluation is a component of risk assessment that involves gathering and evaluating data on the types of health injuries or diseases (e.g., cancer) that may be produced by a chemical and on the conditions of exposure under which such health effects are produced. See Terms of Environment at: http://iaspub.epa.gov/sor_internet/registry/termreg/searchandretrieve/termsandacronyms/search.do.

In total, the EPA identified 1,173 chemicals as being used in hydraulic fracturing fluid and/or detected in flowback and produced water. The complete list of chemicals and associated data is available in Appendices A and B.[1]

9.2.1. Chemicals Used in Hydraulic Fracturing Fluids

Of the 1,173 total chemicals, the EPA identified 1,076 chemicals as being used in hydraulic fracturing fluids. Of these, 692 chemicals were listed in the FracFocus database, and therefore had information available in order to calculate their nationwide frequency of use (U.S. EPA, 2015a).[2] Frequency of use for individual chemicals ranged from low (481 chemicals on the list were used in less than 1% of wells nationwide) to very high (methanol was used in 73% of wells nationwide). Furthermore, only 32 chemicals (excluding water, quartz, and sodium chloride) were reported in at least 10% of the disclosures nationwide (see Section 5.4 and Table 5-2). As noted previously, the FracFocus database does not list or consider those chemicals identified as CBI. The EPA determined that approximately 70% of the disclosures in the FracFocus database contain at least one CBI chemical, and for those disclosures, the average number of CBI chemicals per disclosure was five (see Section 5.4, Text Box 5-3). Additionally, as noted previously, approximately 35% of FracFocus ingredient records were not able to be assigned standardized chemical names. These ingredient records were excluded from the EPA's analysis (see Section 5.10).

9.2.2. Chemicals Detected in Flowback and Produced Water

Of the 1,173 total chemicals, 134 were identified as having been detected in flowback or produced water. Included among these chemicals are naturally occurring organic compounds, metals, radionuclides, and pesticides. As reported in Chapter 7, concentration data in flowback or produced water are available for 75 of these 134 chemicals (see Appendix E), including inorganic contributors to salinity (Tables E-4 and E-5), metals (Tables E-6 and E-7), radioactive constituents (Table E-8), and organic constituents (Tables E-9, E-10, and E-11). For these chemicals with concentration data, the measured concentrations spanned several orders of magnitude. For instance, for organic chemicals in produced water from the Marcellus shale formation (Table E-10), average or median measured concentrations ranged from 2.7 μg/L for N-nitrosodiphenylamine to 400 μg/L for carbon disulfide. According to the sources listed in Appendix A, 37 of the total 134 chemicals in flowback and produced water were also identified as being used in hydraulic fracturing fluid.

9.3. Toxicological and Physicochemical Properties of Hydraulic Fracturing Chemicals

Toxicological and physicochemical data were collected as available for each of the chemicals identified in Appendix A. The criteria used to identify and select toxicity values, RfVs and OSFs (Section 9.3.1), and the method used to generate physicochemical property data (Section 9.3.2) are discussed below. A summary of the available data for these chemicals follows in Section 9.3.3. Other

[1] The list of 1,173 chemicals was finalized as of this 2015 draft assessment. There may be chemicals present in flowback and produced water that are not included on this list.
[2] The FracFocus frequency of use data presented in this chapter is based on 35,957 well disclosures.

possible sources of toxicological information, including QSAR-approaches and the EPA's ACToR database, are discussed in Section 9.3.4.

9.3.1. Selection of Toxicity Values: Reference Values (RfVs) and Oral Slope Factors (OSFs)

Toxicity information spans a wide range with respect to extent, quality and reliability. Toxicological data may include assessments from various sources including state, national, international, private and academic organizations as well as toxicity information which has not been formalized into an assessment and may be found in the scientific literature and databases including results from guideline tests, high throughput screening assays, alternative assays, and QSAR models. The sources of toxicity values – specifically, chronic oral RfVs and OSFs – selected for the purposes of this chapter are based on criteria developed specifically for this report. For many of the chemicals used in hydraulic fracturing or found in flowback or produced water there may be relevant information, including cancer and noncancer-related information, from one or more sources that were not evaluated in this chapter.

The sources of RfVs and OSFs selected for the purposes of this chapter met the following key criteria: 1) the body or organization generating or producing the peer-reviewed RfVs, peer-reviewed OSFs, or peer-reviewed qualitative assessment must be a governmental or intergovernmental body; 2) the data source must include peer-reviewed RfVs, peer-reviewed OSFs, or peer reviewed qualitative assessments; 3) the RfVs, OSFs, or qualitative assessments must be based on peer-reviewed scientific data; 4) the RfVs, OSFs, or qualitative assessments must be focused on protection of the general public; and 5) the body generating the RfVs, OSFs, or qualitative assessments must be free of conflicts of interest with respect to the chemicals for which it derives reference values or qualitative assessments. More detail on these criteria for selection and inclusion of data sources, as well as the full list of data sources that were considered for this study, are available in Appendix G.

RfVs and OSFs available from the EPA IRIS, the EPA PPRTV program, ATSDR, and the EPA HHBP program all met the criteria for selection and inclusion as a data source (see Table 9-1). An attempt was made to identify and acquire RfVs and OSFs from all 50 states, but only the peer-reviewed state RfVs and OSFs from California met the stringent selection criteria and were included because of the state's extensive peer review process.[1] One international source for RfVs, the World Health Organization's (WHO) International Programme on Chemical Safety (IPCS) Concise International Chemical Assessment Documents (CICAD), also met the selection criteria. The International Agency for Research on Cancer (IARC) and U.S. National Toxicology Program (NTP) Report on Carcinogens also met the criteria and were used as additional sources for qualitative cancer classifications.

Table 9-1. Sources of selected toxicityRfVs and OSFs.

Source	Website

[1] State RfVs and OSFs are also publicly available from Alabama, Texas, Hawaii, and Florida, but they did not meet the criteria for consideration as sources for RfVs and OSFs in this report. See Appendix G for details.

Source	Website
EPA Integrated Risk Information System (IRIS)	http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showSubstanceList
Human Health Benchmarks for Pesticides (HHBP)	http://iaspub.epa.gov/apex/pesticides/f?p=HHBP:home
EPA Provisional Peer-Reviewed Toxicity Value (PPRTV) database	http://hhpprtv.ornl.gov/index.html
Agency for Toxic Substances and Disease Registry (ATSDR) Minimum Risk Levels	http://www.atsdr.cdc.gov/toxprofiles/index.asp#bookmark05
State of California Toxicity Criteria Database	http://www.oehha.org/tcdb/index.asp
International Programme on Chemical Safety (IPCS) Concise International Chemical Assessment Documents (CICAD)	http://www.who.int/ipcs/publications/cicad/en/

EPA generally applies federal RfVs and OSFs for use in human health risk assessments. Therefore, for the purpose of hazard evaluation and making comparisons between chemicals in this chapter, only federal chronic oral RfVs and OSFs from the EPA IRIS, the EPA PPRTV program, ATSDR, and the EPA HHBP program were used. Furthermore, when a chemical had an RfV and/or OSF from more than one federal source, a modification of the EPA Office of Solid Waste and Emergency Response (OSWER) Directive 9285.7-53 tiered hierarchy of toxicity values was applied to determine which value to use. A single RfV and/or OSF was selected from the sources in this order: IRIS, HHBP, PPRTV, and ATSDR.[1] The RfVs considered from these sources included noncancer reference doses (RfDs) from the IRIS, PPRTV, and HHBP programs, and oral minimum risk levels (MRLs) from ATSDR.[2,3]

Because there are relatively few OSFs available compared to RfVs, OSFs were excluded from discussion in this chapter; however, all available OSFs are reported in Appendix G. The EPA drinking water maximum contaminant levels (MCLs) were also excluded from this analysis because they are treatment-based. MCLs are set as close to maximum containment level goal (MCLG) values as feasible. However, MCL and MCLGs values are still reported in Appendix G for the sake of completeness.

[1] The OSWER hierarchy indicates that sources should be used in this order: IRIS, PPRTV, and then other values. In this report, this hierarchy was followed, but HHBP values were used in lieu of an IRIS value for a few chemicals. See Appendix G for details.

[2] A RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. For the complete definition see Appendix G.

[3] An MRL is an estimate of daily human exposure to a hazardous substance at or below which the substance is unlikely to pose a measurable risk of harmful (adverse), noncancerous effects. MRLs are calculated for a route of exposure (inhalation or oral) over a specified time period (acute, intermediate, or chronic). MRLs should not be used as predictors of harmful (adverse) health effects. Chronic MRL: Duration of exposure is 365 days or longer.

9.3.2. Physicochemical Properties

As presented in Chapter 5, EPI Suite™ software was used to generate data on the physicochemical properties of chemicals on the consolidated list. EPI Suite™ provides an estimation of physicochemical properties based upon chemical structure, and will additionally provide empirically measured values for these properties when they are available for a given chemical. For more details on the software and on the use of physicochemical properties for fate and transport estimation, see Chapter 5.

9.3.3. Summary of Selected Toxicological and Physicochemical Property Data for Hydraulic Fracturing Chemicals

Figure 9-1 summarizes the availability of selected RfVs and OSFs and physicochemical data for the 1,173 hydraulic fracturing chemicals identified by the EPA.

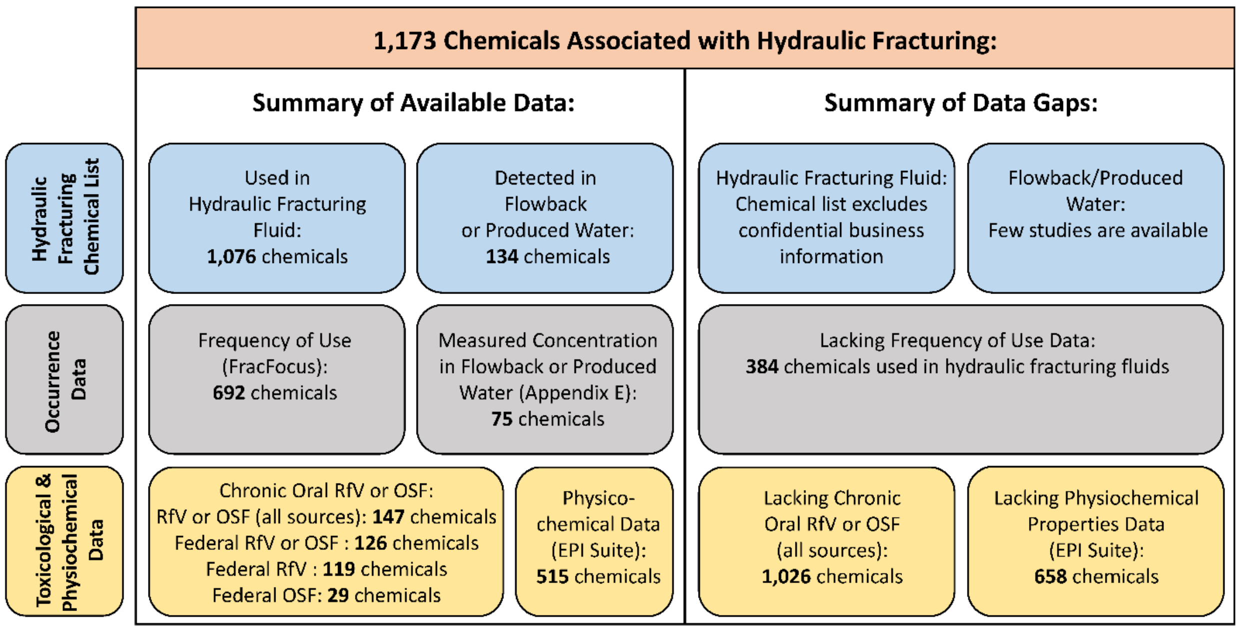

Figure 9-1. Overall representation of the selected RfVs and OSFs, occurrence data, and physicochemical data available for the 1,173 hydraulic fracturing chemicals identified by the EPA.

Of the 1,173 chemicals identified by the EPA, only 147 (13%) have federal, or state, or international chronic oral RfVs and/or OSFs from sources listed in Table 9-1. Therefore, chronic RfVs and/or OSFs from the selected sources are lacking for 87% of chemicals that the EPA has identified as associated with hydraulic fracturing. All available chronic RfVs and OSFs from the sources listed in Table 9-1 are tabulated in Appendix G. Chronic RfVs and OSFs for chemicals used in hydraulic fracturing fluids are listed in Tables G-1a through G-1c, and chronic RfVs and OSFs for chemicals reported in hydraulic fracturing flowback and produced water are listed in Tables G-2a through G-2c.

From the U.S. federal sources that were considered here, the availability of chronic RfVs and OSFs can be summarized as follows. Of the 1,173 chemicals on the consolidated list, a total of 126 chemicals have federal chronic RfVs and/or OSFs. Of these 126 chemicals, 119 have federal chronic RfVs, and 29 have federal OSFs (see Figure 9-1). 22 chemicals have both a federal chronic RfV and a federal OSF, while 7 have a federal OSF only.

Overall, when chemicals in hydraulic fracturing fluid and chemicals in flowback are considered separately, the availability of chronic RfVs and OSFs can be summarized as follows:

- For the 1,076 chemicals used in hydraulic fracturing fluid, chronic RfVs from all of the selected federal, state, and international sources were available for 90 chemicals (8.4%). From the federal sources alone, chronic RfVs were available for 73 (6.8%), and OSFs were available for 15 (1.4%).

- For the 134 chemicals reported in flowback and produced water, chronic RfVs from all of the selected federal, state, and international sources were available for 83 chemicals (62%). From the federal sources alone, chronic RfVs were available for 70 chemicals (52%), and OSFs were available for 20 (15%).

The IRIS database was the most abundant source of the federal chronic RfVs and OSFs. IRIS had available RfDs for 77 of the total 1,173 chemicals, and OSFs for 27 chemicals. Of the other federal data sources, the PPRTV database had RfDs for 33 chemicals, and OSFs for 2 chemicals; the HHBP database had RfDs for 11 chemicals, but did not have available OSFs for any of the chemicals; and the ATSDR database had chronic oral MRLs for 27 chemicals.

In addition to these chronic values, many of the chemicals also have less-than-chronic federal oral RfVs. Subchronic or acute federal RfVs were identified for 91 chemicals on the consolidated list, including 55 chemicals used in hydraulic fracturing fluid (Table G-1d), and 56 chemicals reported in flowback or produced water (Table G-2d). There were 8 chemicals that had less-than-chronic RfVs but lacked a chronic RfV. All of these less-than-chronic RfVs were found on the PPRTV or ATSDR databases; the IRIS database did not have less-than-chronic RfVs for any of these chemicals. These values are not discussed in this report, but are provided in Appendix G as supporting information.

From the total list of 1,173 chemicals associated with hydraulic fracturing, EPI Suite™ was able to generate data on physicochemical properties for 515 (44%) of the chemicals (see Appendix A). The remaining 658 chemicals lacked the structural information necessary to generate an estimate.

9.3.4. Additional Sources of Toxicity Information

Because the majority of chemicals identified in this report do not have RfVs and/or OSFs from the selected sources, it is likely that risk assessors at the local and regional level may turn to alternative sources of toxicity information. This section discusses other publicly accessible sources of toxicological data that are lower on the continuum of quality and reliability in comparison to the selected RfVs and OSFs described above. Because the quality of these data is unknown for most chemicals, values from these data sources are not included in the hazard evaluation in this report.

9.3.4.1. Estimated Toxicity Using Quantitative Structure Activity Relationships (QSAR)

One potential source of toxicological information is QSAR software, which is able to provide estimates or predictions of toxicity based on chemical structure. QSAR models for toxicity have been used and evaluated in a number of previous studies published in the peer reviewed literature (Rupp et al., 2010; Venkatapathy et al., 2004; Moudgal et al., 2003). A key advantage to QSAR models is that they are able to rapidly and inexpensively estimate toxicity values for chemicals. Compared to toxicological studies involving animals or in vitro methods, which have monetary, time, and ethical considerations associated with them, the QSAR method requires only information on chemical structure in order to generate a toxicity estimation. These values may be of lower quality and less reliable than values generated using traditional toxicological methods. However, because they increase the available pool of toxicity information, QSAR estimates may potentially be a useful resource for risk assessors that are faced with evaluating potential exposures to data-poor chemicals.

9.3.4.2. Chemical Data Available from ACToR

An additional tool for obtaining toxicological information is the ACToR database.[1] ACToR is a large data warehouse developed by the EPA to gather and house large and disparate amounts of public data on chemicals including chemical identity, structure, physicochemical properties, in vitro assay results, and in vitro toxicology data (Judson et al., 2009). ACToR contains data on over 500,000 chemicals from over 2,500 sources, covering many domains including hazard, exposure, risk assessment, risk management, and use. Data in ACToR is organized on several levels of "assays" and "assay categories". The information available in ACToR ranges from the federal RfVs and OSFs discussed in Section 9.3.1, which have undergone extensive peer review, to other toxicity values and study and test results that have undergone little to no peer review.

The ACToR database was searched for information related to the total list of 1,173 chemicals associated with hydraulic fracturing.[2] For the purposes of this chapter, the database was first searched for all of the assays and assay categories that had data on these chemicals. This initial search was then filtered to only include the assay categories that are most relevant to toxicity via the oral route of exposure (drinking water). These assay categories were assigned into the following nine data classes: carcinogenicity, dose response values, drinking water criteria, genotoxicity/mutagenicity, hazard identification, LOAEL/NOAEL, RfD, slope factor, and water quality criteria. The type of data and examples of the data sources included in these data classes can be found in the ACToR database documentation.

When all assays and assay categories were considered, it was found that all but 28 of the total 1,173 chemicals had available data on ACToR. When only the relevant assays and assay categories were considered, 642 (55%) of the chemicals were found to have data on ACToR. The fraction of

[1] The ACToR database is available at: http://actor.epa.gov.
[2] The ACToR database was queried for the total list of 1,173 chemicals on April 1, 2015.

chemicals that had at least one data point in each of the nine ACToR data classes is shown in Figure 9-2. As can be seen in Figure 9-2, about half of the chemicals had some information on water quality criteria, while fewer chemicals had information on the other classes of data.

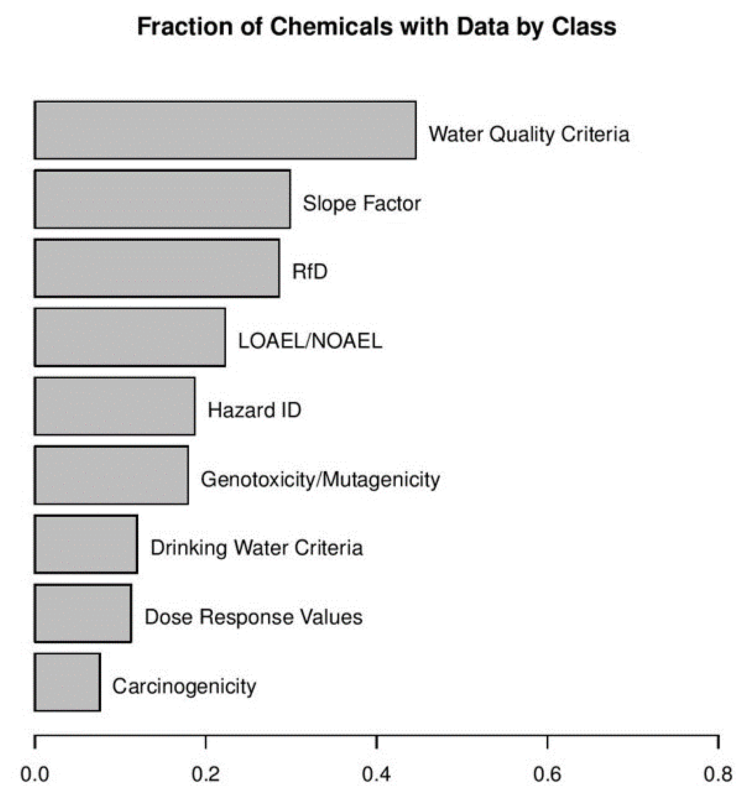

Figure 9-2. Fraction of chemicals with at least one data point in each ACToR data class.

Focusing on the 1,026 chemicals that lacked a chronic RfV and/or OSF from the selected sources described in Section 9.3.1, 497 (48%) of these chemicals had available data on ACToR. Because ACToR has a significant amount of data on potential chemical hazards, including for some data-poor chemicals, ACToR might help to fill data gaps in the ongoing effort to understand potential hazards of hydraulic fracturing chemicals. Since the quality of the non-peer reviewed values is not known, these data are not considered in the hazard evaluation.

9.4. Hazard Identification of Reported Hydraulic Fracturing Chemicals

This section focuses on chemicals that were identified as being of particular interest in previous chapters of this report, or which otherwise may be of particular interest to risk assessors. Federal RfVs are identified for these chemicals as available.

9.4.1. Selection of Additional Chemicals for Hazard Identification

Four subsets of chemicals were identified as being of interest in Chapter 5 (Chemical Mixing) and Chapter 7 (Flowback and Produced water):

1. Chapter 5: The most frequently used chemicals in hydraulic fracturing fluid, defined as chemicals being reported to the FracFocus database in at least 10% of well disclosures (U.S. EPA, 2015a).
2. Chapter 5: The top 20 most and least mobile chemicals from the EPA's analysis of the FracFocus database (U.S. EPA, 2015a), as determined based on the octanol-water partition coefficient (K_{ow}) from EPI Suite™.
3. Chapter 7: Inorganic chemicals that may be returned to the surface in flowback and produced water. This includes metals, inorganic ions, and naturally occurring radioactive material (NORM).
4. Pesticides occurring in flowback and produced water.

The hazard identification for these four subsets of chemicals is presented below.

9.4.2. Hazard Identification Results

9.4.2.1. Most Frequently Used Chemicals in Hydraulic Fracturing Fluid (FracFocus)

Chapter 5 listed 35 chemicals that are reported to the FracFocus database in at least 10% of well disclosures nationwide (U.S. EPA, 2015a) (Table 5-2). For 32 of these chemicals (water, quartz, and sodium chloride were excluded from this analysis), only 7 chemicals (22%) have a federal chronic RfV, as shown in Table 9-2. None of these 32 chemicals have available OSFs for cancer. For this subset of chemicals, methanol was reported to be the most frequently used chemical in the FracFocus analysis, followed by hydrotreated light petroleum distillates and hydrochloric acid, all of which were reported in greater than 60% of disclosures. Ethylene glycol, isopropanol, and peroxydisulfuric acid-diammonium salt are the only 3 additional chemicals to have been used in greater than 40% of disclosures.

Table 9-2. List of the most frequently used chemicals in hydraulic fracturing fluids, with their respective federal chronic RfVs where available.

Chemicals are ordered in the table, from high to low, based on their frequency of use from FracFocus. Includes all chemicals reported to FracFocus in at least 10% of well disclosures, excluding water, quartz, and sodium chloride.

Chemical	CASRN	RfV Chronic RfD (mg/kg-day)	Source
Methanol	67-56-1	2	IRIS
Distillates, petroleum, hydrotreated light	64742-47-8	--	--
Hydrochloric acid	7647-01-0	--	--

Chemical	CASRN	RfV	Source
		Chronic RfD (mg/kg-day)	
Ethylene glycol	107-21-1	2	IRIS
Isopropanol	67-63-0	--	
Peroxydisulfuric acid, diammonium salt	7727-54-0	--	--
Guar gum	9000-30-0	--	--
Sodium hydroxide	1310-73-2	--	--
Propargyl alcohol	107-19-7	0.002	IRIS
Glutaraldehyde	111-30-8	--	--
Ethanol	64-17-5	--	--
Potassium hydroxide	1310-58-3	--	--
Acetic acid	64-19-7	--	--
Citric acid	77-92-9	--	--
2-Butoxyethanol	111-76-2	0.1	IRIS
Solvent naphtha, petroleum, heavy arom.	64742-94-5	--	--
Naphthalene	91-20-3	0.02	IRIS
2,2-Dibromo-3-nitrilopropionamide	10222-01-2	--	--
Choline chloride	67-48-1	--	--
Phenolic resin	9003-35-4	--	--
Methenamine	100-97-0	--	--
Carbonic acid, dipotassium salt	584-08-7	--	--
1,2,4-Trimethylbenzene	95-63-6	--	--
Quaternary ammonium compounds, benzyl-C12-16-alkyldimethyl, chlorides	68424-85-1	--	--
Poly(oxy-1,2-ethanediyl)-nonylphenyl-hydroxy (mixture)	127087-87-0	--	--
Formic acid	64-18-6	0.9	PPRTV
Sodium chlorite	7758-19-2	0.03	IRIS
Nonyl phenol ethoxylate	9016-45-9	--	--
Tetrakis(hydroxymethyl)phosphonium sulfate	55566-30-8	--	--
Polyethylene glycol	25322-68-3	--	--
Ammonium chloride	12125-02-9	--	--
Sodium persulfate	7775-27-1	--	--

9.4.2.2. Most and Least Mobile Chemicals Used in Hydraulic Fracturing Fluid (FracFocus)

Chapter 5 lists the 20 most mobile chemicals (Table 5-7) and 20 least mobile chemicals (Table 5-8) from the EPA's analysis of the FracFocus database (U.S. EPA, 2015a). For these lists, mobility was determined based on K_{ow}. For the 20 most mobile chemicals, no federal chronic RfVs or OSFs were available (see Table 9-3). Similarly, for the 20 least mobile chemicals, only one chemical—di(2-ethylhexyl) phthalate—had a federal chronic RfV available (see Table 9-4).

Table 9-3. List of the 20 most mobile chemicals used in hydraulic fracturing fluid, with their respective federal chronic RfVs where available.

Chemicals are ordered in the table by lowest estimated log K_{ow}. None of these chemicals had federal chronic RfVs available.

Chemical	CASRN	Log K_{ow} (unitless)	RfV	Source
			Chronic RfD (mg/kg-day)	
1,2-Ethanediaminium, N,N'-bis[2-[bis(2-hydroxyethyl)methylammonio]ethyl]-N,N'-bis(2-hydroxyethyl)-N,N'-dimethyl-, tetrachloride	138879-94-4	-23.19	--	--
Phosphonic acid, [[(phosphonomethyl)imino] bis[2,1-ethanediylnitrilobis (methylene)]]tetrakis-	15827-60-8	-9.72	--	--
Phosphonic acid, [[(phosphonomethyl)imino] bis[2,1-ethanediylnitrilobis (methylene)]]tetrakis-, sodium salt	22042-96-2	-9.72	--	--
Phosphonic acid, [[(phosphonomethyl)imino] bis[2,1-ethanediylnitrilobis (methylene)]]tetrakis-, ammonium salt (1:x)	70714-66-8	-9.72	--	--
Phosphonic acid, (((2-[(2-hydroxyethyl)(phosphono methyl)amino)ethyl)imino]bis (methylene))bis-, compd. with 2-aminoethanol	129828-36-0	-6.73	--	--
2-Hydroxy-N,N-bis(2-hydroxyethyl)-N-methylethanaminium chloride	7006-59-9	-6.7	--	--
N-(3-Chloroallyl)hexaminium chloride	4080-31-3	-5.92	--	--
3,5,7-Triazatricyclo(3.3.1.1(superscript 3,7))decane, 1-(3-chloro-2-propenyl)-, chloride, (Z)-	51229-78-8	-5.92	--	--
(2,3-dihydroxypropyl)trimethylammonium chloride	34004-36-9	-5.8	--	--
Phosphonic acid, [[(phosphonomethyl)imino] bis[6,1-hexanediylnitrilobis(methylene)]]tetrakis-	34690-00-1	-5.79	--	--

Chemical	CASRN	Log K_{ow} (unitless)	RfV Chronic RfD (mg/kg-day)	Source
[Nitrilotris(methylene)]tris-phosphonic acid pentasodium salt	2235-43-0	-5.45	--	--
Aminotrimethylene phosphonic acid	6419-19-8	-5.45	--	--
Choline chloride	67-48-1	-5.16	--	--
Choline bicarbonate	78-73-9	-5.16	--	--
alpha-Lactose monohydrate	5989-81-1	-5.12	--	--
Lactose	63-42-3	-5.12	--	--
Tetrakis(hydroxymethyl)phosphonium sulfate	55566-30-8	-5.03	--	--
Disodium ethylenediaminediacetate	38011-25-5	-4.76	--	--
Nitrilotriacetamide	4862-18-4	-4.75	--	--
1,3,5-Triazine-1,3,5(2H,4H,6H)-triethanol	4719-04-4	-4.67	--	--

Table 9-4. List of the 20 least mobile chemicals used in hydraulic fracturing fluid, with their respective federal chronic RfVs where available.

Chemicals are ordered in the table by highest estimated log K_{ow}.

Chemical	CASRN	Log K_{ow} (unitless)	RfV Chronic RfD (mg/kg-day)	Source

Chemical	CASRN	Log K_{ow} (unitless)	RfV Chronic RfD (mg/kg-day)	Source
Sorbitan, tri-(9Z)-9-octadecenoate	26266-58-0	22.56	--	--
Fatty acids, C18-unsatd., dimers	61788-89-4	14.6	--	--
Sorbitan sesquioleate	8007-43-0	14.32	--	--
Tributyltetradecylphosphonium chloride	81741-28-8	11.22	--	--
Sodium bis(tridecyl) sulfobutanedioate	2673-22-5	11.15	--	--
1-Eicosene	3452-07-1	10.03	--	--
D&C Red 28	18472-87-2	9.62	--	--
C.I. Solvent Red 26	4477-79-6	9.27	--	--
1-Octadecene	112-88-9	9.04	--	--
Alkenes, C>10 .alpha.-	64743-02-8	8.55	--	--
Dioctyl phthalate	117-84-0	8.54	--	--
Benzene, C10-16-alkyl derivs.	68648-87-3	8.43	--	--
Di(2-ethylhexyl) phthalate	117-81-7	8.39	0.02	IRIS
1-Octadecanamine, N,N-dimethyl-	124-28-7	8.39	--	--
N,N-dimethyloctadecylamine hydrochloride	1613-17-8	8.39	--	--
Butyryl trihexyl citrate	82469-79-2	8.21	--	--
1-Hexadecene	629-73-2	8.06	--	--
Benzo(g,h,i)perylene	191-24-2	7.98	--	--
Dodecylbenzene	123-01-3	7.94	--	--
Isopropanolamine dodecylbenzene	42504-46-1	7.94	--	--

9.4.2.3. Flowback and Produced Water: Inorganics and NORM

In addition to a number of volatile and semi-volatile organic compounds presented below, Chapter 7 also discusses the appearance of inorganic constituents such as metals, inorganic ions, and naturally occurring radioactive material (NORM) in flowback and produced water. A number of metals detected in flowback and produced water that appear on the EPA's consolidated list and are noted in Chapter 7 have federal RfVs and/or OSFs listed in Appendix G (Table G-2). These metals and inorganic ions include: iron, boron, chromium, zinc, arsenic, manganese, cadmium, and strontium. These metals have oral RfVs based on a number of health effects including: neurotoxicity, developmental and liver toxicity, hyperpigmentation and keratosis of the skin, and decrements in blood copper status and enzyme activity. Chromium (VI) is classified as a known human carcinogen by IARC and NTP, while arsenic is classified as known human carcinogen by the EPA, IARC, and NTP. Radionuclides, such as radium-226, radium-228, and uranium-238, which are naturally occurring in the formation may also return to the surface within produced water. Each of these radionuclides is classified as a known human carcinogen by the EPA and IARC.

9.4.2.4. Flowback and Produced Water: Pesticides

Lastly, it should be noted that a number of pesticides appear in the tables presented in Appendix G. These chemicals were reported as having been detected in analyses of hydraulic fracturing flowback and produced waters by several of the 10 sources cited in Appendix A; however, there is much uncertainty about why they were detected. They could have migrated to the shale formation or to the rock surrounding the shale formation, or they could have migrated into source waters used by the hydraulic fracturing operation. It is also possible that these are laboratory contaminants.

9.5. Hazard Identification and Hazard Evaluation of Selected Subsets of Hydraulic Fracturing Chemicals

As described in Section 9.4, the majority of chemicals identified in the previous chapters of this report do not have RfVs and/or OSFs from the sources meeting the criteria described in Section 9.3.1. This lack of data creates a challenge for hazard evaluation, because the potential human health effects of these chemicals are difficult to determine. On the other hand, other chemicals identified by the EPA have more data available, including chronic RfVs, data on occurrence, and data on physicochemical properties. This section focuses on the hazard evaluation of these subsets of chemicals that had data available.

When considering the hazard evaluation of chemicals in drinking water, it is important to remember that toxicity is contingent upon exposure. All chemicals, including pure water, may be toxic if they are ingested in large enough quantities. Therefore, in addition to data on health effects, hazard evaluations must also consider data on potential chemical exposure. In the context of the hazard evaluation presented in this section, chemical occurrence and physicochemical property data were used as metrics to estimate the likelihood that the chemical could reach and impact drinking water resources.

For the selected subsets of chemicals that had data available, this section discusses the known toxicological properties based on selected RfVs (hazard identification), and then illustrates one possible method for combining toxicity and exposure potential information for a more data-informed hazard evaluation. Additionally, this section presents a summary of chemicals that have occurrence data across multiple stages of the hydraulic fracturing water cycle.

9.5.1. Selection of Chemicals for Hazard Evaluation

From the overall list of 1,173 chemicals identified in this assessment, subsets of chemicals were selected for hazard evaluation if they met the following criteria:

1. Had a federal chronic oral RfV;

2. Had available data on frequency of use (in hydraulic fracturing fluids) or measured concentrations (in flowback and produced water); and
3. Had available data on physicochemical properties.

These criteria were selected for hazard evaluation for the following reasons:

1. Federal RfVs generally undergo more extensive independent peer review compared to other sources of RfVs. Additionally, as described above, there are many more chemicals with federal chronic RfVs than chemicals with federal OSFs. Therefore, although OSFs are discussed in the hazard evaluation, chronic RfVs were selected for illustrative purposes of making comparisons between chemicals.
2. Data on frequency of use (in hydraulic fracturing fluids) or measured concentration (in flowback or produced water) provide a metric to help assess the likelihood of chemical occurrence in the hydraulic fracturing water cycle. Chemicals that are used more frequently in hydraulic fracturing fluid have a greater likelihood of accidental release or dissemination due to the fact that they are present at a greater number of wells nationwide. Likewise, chemicals that occur at higher concentrations in flowback or produced water may result in greater exposures. Frequency of detection in flowback or produced water would also be a useful metric for this evaluation, but this information was not available for these chemicals.
3. Information on physicochemical properties enables the estimation of chemical persistence and mobility in the environment. This is discussed in more detail in Section 9.5.2 below.

For chemicals that are used in hydraulic fracturing fluids, the FracFocus database was the only source with reliable information on the frequency of use (U.S. EPA, 2015a). For chemicals found in flowback or produced water, data on measured concentration were only available for the 75 chemicals presented in Appendix E. Therefore, hazard evaluations were only conducted on chemicals included in these two data sources. While the other data sources listed in Appendix A provide useful information on the diversity of chemicals that may occur in the hydraulic fracturing water cycle, hazard evaluation could not be conducted on these sources in the absence of data on frequency of use or measured concentration.

Overall, 37 chemicals used in hydraulic fracturing fluid and 23 chemicals detected in flowback and produced water met the selection criteria for hazard evaluation (see Figure 9-3).

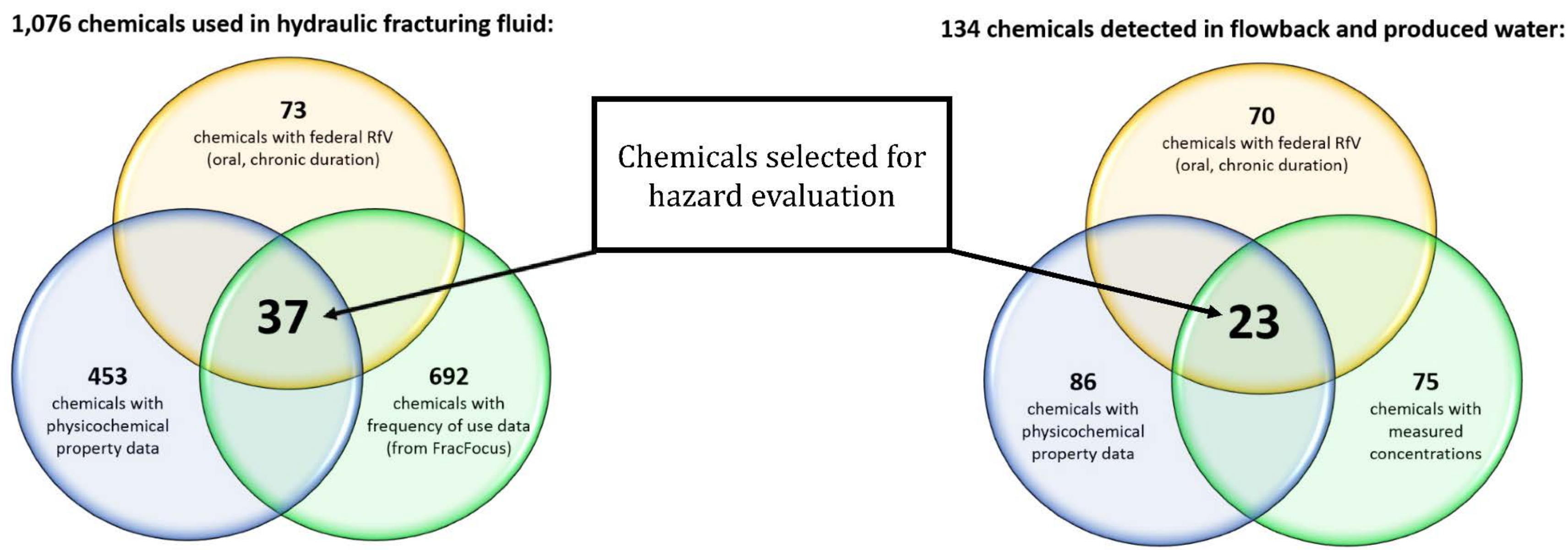

Figure 9-3. The two subsets of chemicals selected for hazard evaluation included 37 chemicals used in hydraulic fracturing fluid, and 23 chemicals detected in flowback or produced water.

9.5.2. Multi Criteria Decision Analysis (MCDA) Framework for Hazard Evaluation: Integrating Toxicity, Occurrence, and Physicochemical Data

Integration or combining of various types of data may provide insights on those chemicals that may be of greater concern than other chemicals to drinking water resources. For the purpose of this chapter, a structured but flexible Multi Criteria Decision Analysis (MCDA) approach was developed to integrate factors related to hydraulic fracturing such as chemical toxicity, occurrence, and physicochemical data. The approach described here is for illustrative purposes only, in order to demonstrate how combining of information may be informative. Alternative frameworks may be considered by risk assessors for similar analyses.

In this illustration, a MCDA framework was developed and applied to each list of chemicals identified in Section 9.5.1 and depicted in Figure 9-3 (37 chemicals used in hydraulic fracturing fluids, and 23 chemicals detected in flowback or produced water). The MCDA framework serves to place the toxicity of these chemicals in the context of factors that may increase the likelihood of impacting drinking water resources. In essence, this analysis serves to illustrate the circumstances under which drinking water resources may be affected.

MCDA is a well-established analysis tool that is used to transparently integrate multiple lines of evidence to support decision-making. For example, MCDA has been adapted as a method of selecting an optimal cleanup plan for a contaminated site (Linkov et al., 2011), and as a method of integrating chemical hazard data across multiple studies (Hristozov et al., 2014). The MCDA framework employed here is based on the method by Mitchell et al. (2013b), who developed a protocol for ranking chemical exposure potential by integrating data on physicochemical properties and commercial use. This method is similar to approaches used by the petroleum industry to quantitatively rank the potential hazards of hydraulic fracturing chemicals (see Section 5.9). Moreover, the underlying philosophy of this approach is similar to that of the EPA's Design for the Environment (DfE) Program. The DfE's Alternatives Assessment Criteria for Hazard Evaluation (U.S. EPA, 2011a) was developed as a tool for evaluating and differentiating among chemical hazards based on toxicity and physicochemical properties. Recently, this criteria and framework have been applied in the Alternatives Assessment for the Flame Retardant Decabromodiphenyl Ether (DecaBDE) and Flame Retardant Alternatives for Hexabromocyclododecane (HBCD) (U.S. EPA, 2014a, d). Aspects of MCDA methods and the DfE's Program for Alternatives Assessment are evident in the National Research Council (NRC)'s "A Framework to Guide Selection of Chemical Alternatives" document (NRC, 2014).

The methodology used to illustrate a hazard evaluation MCDA for hydraulic fracturing is outlined below, and schematic of the model is shown in Figure 9-4. Under the MCDA framework, each chemical was assigned three scores:

1. A toxicity score;
2. An occurrence score; and
3. A physicochemical properties score.

The three normalized scores were summed to develop a total composite hazard potential score for each chemical. These scores serve as a relative ranking and a means of making comparisons across chemicals. These scores are not intended to define whether or not a chemical will present a human health hazard, or indicate that one chemical is safer than another. Rather, the scores serve as a qualitative metric to identify chemicals that may be more likely to present an impact to drinking water resources, given available data on chemical properties and occurrence.

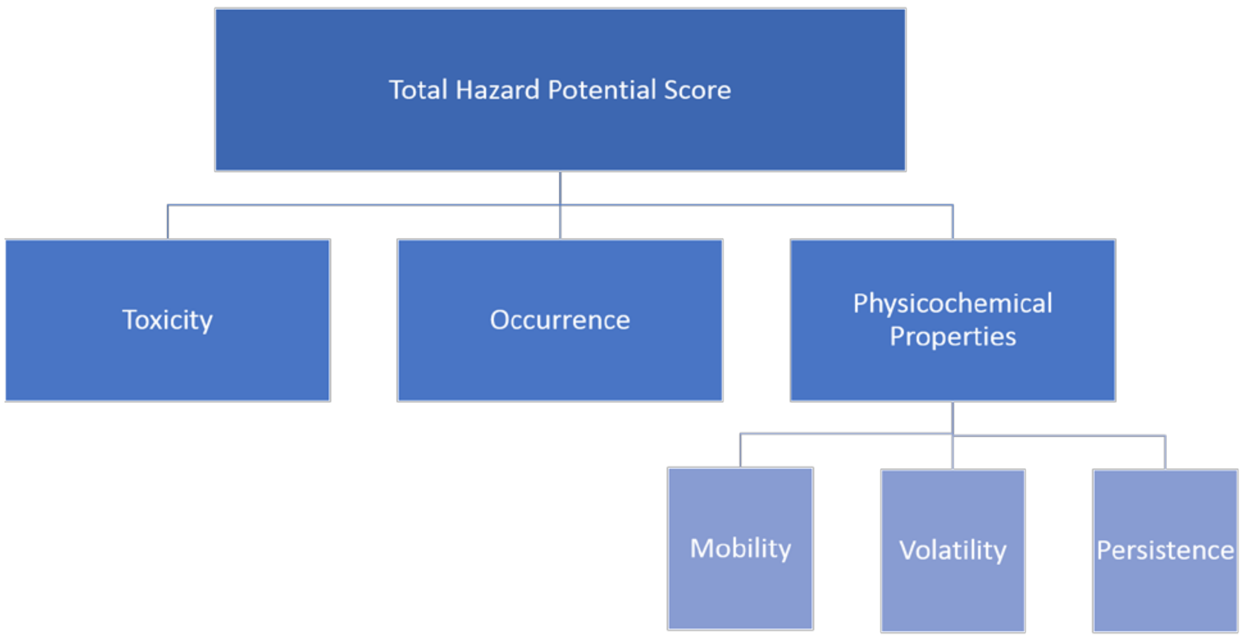

Figure 9-4. Overview of the MCDA framework applied to the hazard evaluations.

9.5.2.1. Toxicity Score

The toxicity score was based upon the federal chronic RfV, which was determined from peer reviewed sources as described in Section 9.3.1. Within each dataset (chemicals used in hydraulic fracturing fluids, or chemicals detected in flowback and produced water), toxicity was ranked based on quartiles, with each chemical assigned a toxicity score of 1 to 4 (see thresholds outlined in Table 9-5). Note that chemicals in the lowest quartile received the highest toxicity score as these chemicals have lower RfVs than for other chemicals.

9.5.2.2. Occurrence Score

This score was based on the frequency or concentration at which chemicals were reported within the hydraulic fracturing water cycle. For chemicals used in hydraulic fracturing fluids, the occurrence score was based on the nationwide number of well disclosures for each chemical from the FracFocus database. For chemicals that were detected in hydraulic fracturing flowback and produced water, the occurrence score was based on the average or median measured concentration reported in Appendix E. If the measured concentration of a chemical was reported by multiple studies in Appendix E, the highest of these reported average or median concentrations was used for this calculation. Note that these two metrics of chemical occurrence—frequency of use, and concentration—cannot be directly compared to one another. Therefore, FracFocus chemicals and flowback and produced water chemicals were considered separately for this MCDA hazard evaluation. Within each dataset (chemicals used in hydraulic fracturing fluids, or chemicals detected in flowback and produced water), chemical occurrence was ranked based on quartiles, with each chemical assigned an occurrence score of 1 to 4, as shown in Table 9-5.

9.5.2.3. Physicochemical Properties Score

This score was based upon inherent physicochemical properties which affect the likelihood that a chemical will reach and impact drinking water resources. The thresholds chosen for ranking physicochemical properties, shown in Table 9-5, are based on previously published thresholds used in the DfE Alternatives Assessment Criteria for Hazard Evaluation (U.S. EPA, 2011a), the EPA Office of Pollution Prevention and Toxics Pollution Prevention (P2) Framework (U.S. EPA, 2005), and Mitchell et al. (2013b). When refining EPI Suite™ physicochemical properties data for input into this MCDA, empirically measured values were always used when available. If multiple estimated values were available, the most conservative value (i.e., the value resulting in the highest score according to Table 9-5) was used.

The total physicochemical properties score for each chemical was based upon three subcriteria: mobility in water, volatility, and persistence. Chemical mobility in water was assessed based upon three physicochemical properties: the octanol-water partition coefficient (K_{ow}), the organic carbon-water partition coefficient (K_{oc}), and aqueous solubility. Chemical volatility was assessed based on the Henry's law constant, which describes partitioning of a chemical between water and air. Chemical persistence was assessed based on estimated half-life in water, which describes how long a chemical will persist in water before it is transformed or degraded. Details on the evaluation and physicochemical score calculation are provided in the Chapter Annex, Section 9.8.1. For each chemical, the mobility score, volatility score, and persistence score (each on a scale of 1 to 4) were summed to calculate a total physicochemical score.

9.5.2.4. Final MCDA Score Calculations

Each raw score (toxicity, occurrence, or physicochemical properties), calculated as described above, was standardized by scaling to the highest and lowest raw score within the set of chemicals. The following equation was used:

$$S_{x\_final} = (S_x - S_{min}) / (S_{max} - S_{min})$$

in which S_x is the raw score for a particular chemical x, S_{max} is the highest observed raw score within the set of chemicals, and S_{min} is the lowest observed raw score within the set of chemicals. S_{x_final} is the standardized score for chemical x. Each standardized score (toxicity, occurrence, or physicochemical properties) falls on a scale of 0 to 1. These standardized toxicity, occurrence, and physicochemical properties scores were summed to calculate a total hazard potential score for each chemical. The total hazard potential scores fell on a scale of 0 to 3, with higher scores indicating chemicals that are predicted to be more likely to affect drinking water resources. An example of MCDA score calculation can be found in the Annex, Section 9.8.2.

In the MCDA approach illustrated in this chapter, each factor (toxicity, occurrence, physicochemical properties) was given equal weight in the calculation of the final hazard potential score. This was done in order to prevent subjectivity and avoid biasing the results based on any individual variable that was considered in this analysis. This approach is adaptable, however. Risk assessors may choose to apply alternative weights that place more or less emphasis on the various factors being considered, in order to reflect expert judgement of a variable's relative importance. This MCDA approach may also be adapted to include other variables of interest, such as carcinogenic potential, which were not considered in the MCDA approach illustrated in this chapter.

Table 9-5. Thresholds used for developing the toxicity score, occurrence score, and physicochemical properties score in this MCDA framework.

Score	1	2	3	4
Toxicity Score				
Chronic RfV (federal)	>3rd quartile	>2nd quartile to ≤3rd quartile	>1st quartile to ≤2nd quartile	≤1st quartile
Occurrence Score				
Percentage of wells nationwide	<1st quartile	≥1st quartile to <2nd quartile	≥2nd quartile to <3rd quartile	≥3rd quartile
Concentration (µg/L)	<1st quartile	≥1st quartile to <2nd quartile	≥2nd quartile to <3rd quartile	≥3rd quartile
Physicochemical Properties Score				
Mobility score:				
Log K_{OW}	>5	>3 to 5	>2 to 3	≤2
Log K_{OC}	>4.4	>3.4 to 4.4	>2.4 to 3.4	≤2.4
Aqueous solubility (mg/L)	<0.1	≥0.1 to <100	≥100 to <1000	≥1000
Volatility score:				
Henry's law constant	$>10^{-1}$	$>10^{-3}$ to $\leq 10^{-1}$	$>10^{-5}$ to $\leq 10^{-3}$	$\leq 10^{-5}$
Persistence score:				
Half-life in water (days)	<16	≥16 to <60	≥60 to <180	≥180

9.5.3. Hazard Evaluation Results

Discussed below are the results of the hazard evaluations for each subset of chemicals identified in Section 9.5.1. For each subset of chemicals selected for hazard evaluation, the information presented includes: the available federal chronic oral RfV (hazard identification), followed by highlights of MCDA analyses (hazard evaluation).

For this MCDA illustration, the calculated toxicity scores, occurrence scores, physicochemical properties scores, and total hazard potential scores are provided for chemicals used in hydraulic fracturing fluids and chemicals detected in flowback/produced water, respectively. These individual scores make it possible to visualize the extent to which the total hazard potential ranking of each chemical is driven by each of the variables considered in the MCDA.

9.5.3.1. Hazard Identification: Chemical Used in Hydraulic Fracturing Fluid

As discussed above, a total of 37 chemicals used in hydraulic fracturing fluids were identified for hazard evaluation using the selection criteria described in Section 9.5.1. Some of the chemicals represented include the BTEX chemicals (benzene, toluene, ethylbenzene, xylenes) as well as naphthalene, acrylamide, phenol, 1,2-propylene glycol, ethylene glycol, 2-butoxyethanol, ethyl acetate, and methanol.

These chemicals along with their primary noncancer toxicological properties, including the point-of-departure (POD), total product of uncertainty factors applied, the federal chronic RfV, and the health effect basis for the RfV, are shown in Table 9-6.[1,2] As seen in Table 9-6, all of these chemicals had RfDs available from IRIS, PPRTV, or HHBP. These chemicals induce a variety of adverse outcomes including immune system effects, changes in body weight, changes in blood chemistry, cardiotoxicity, neurotoxicity, liver and kidney toxicity, and reproductive and developmental toxicity. The RfD values within this suite of chemicals range from 0.001−20 mg/kg-day, with (E)-crotonaldehyde having the lowest RfD (0.001 mg/kg-day) and 1,2-propylene glycol having the highest (20 mg/kg-day).

Comparison of RfVs among a set of chemicals requires a more thorough examination. For instance, to derive the final chronic RfD for a given chemical, a number of UFs may be applied to the POD. Briefly, UFs are applied to account for 5 areas of uncertainty: 1) intraspecies variability; 2)

[1] The point-of-departure (POD) is the dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on dose for an estimated incidence or a change in response level from a dose-response model or a NOAEL or LOAEL for an observed incidence, or change in level of response. See http://www.epa.gov/iris/ for more information.

[2] An uncertainty factor is one of several (generally 10-fold) default factors used in operationally deriving the RfV from experimental data. The factors are intended to account for (1) variation in susceptibility among the members of the human population (i.e., inter-individual or intraspecies variability); (2) uncertainty in extrapolating animal data to humans (i.e., interspecies uncertainty); (3) uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure (i.e., extrapolating from subchronic to chronic exposure); (4) uncertainty in extrapolating from a LOAEL rather than from a NOAEL; and (5) uncertainty associated with extrapolation when the database is incomplete. See the IRIS Glossary at: http://www.epa.gov/iris/ for more information.

interspecies uncertainty; 3) extrapolation from a subchronic study; 4) extrapolating from a NOAEL; and 5) an incomplete database. A UF of 1, 3 ($10^{0.5}$), or 10 can be applied for any of these areas of uncertainty depending upon the amount and/or type data available. The maximum total UF that can be applied is 3,000; RfDs are not derived for chemicals that invoke the application of a total UF >3,000 or involves the application of the full 10-fold UF in four or more areas of uncertainty (U.S. EPA, 2002a). Therefore, those chemicals with a lower total uncertainty factor generally have more reliable and robust health effect information. For example, although (E)-crotonaldehyde has the lowest RfD, chemicals such as acrylamide, benzene, and dichloromethane have RfDs within a factor of 10 (0.002–0.006 mg/kg-day) but with much less uncertainty reflected in their values. All three latter chemicals have large data sets with reproducible effects, and dose estimated based on physiologically based pharmacokinetic models (for acrylamide and dichloromethane) or have available human health effect data (for benzene). Thus, a chemical with a low RfD may reflect high uncertainty in the value and not necessarily be the most toxic.

Although only federal RfVs are considered in this hazard evaluation, eight of these chemicals also have federal OSFs. These include acrylamide, benzyl chloride, 1,4-dioxane, 1,3-dichloropropene, benzene, epichlorohydrin, aniline, and dichloromethane. Of these chemicals, acrylamide is the most potent carcinogen. Acrylamide has an OSF of 0.5 per mg/kg-day and is classified as a likely human carcinogen in IRIS (U.S. EPA, 2010). Benzene is the only chemical listed as a known human carcinogen and has a calculated OSF of 0.015 mg/kg-day (U.S. EPA, 2002b). The OSF values for each of these chemicals can be found in Appendix G.

Table 9-6. Toxicological properties of the 37 chemicals used in hydraulic fracturing fluid that were identified for hazard evaluation and MCDA analysis.

Chemicals are ranked, from low to high, based on their respective federal chronic RfVs.

Chemical	CASRN	Point of departure (mg/kg-day)	Total uncertainty factor	RfV Chronic RfD (mg/kg-day)	Noncancer effect	Source
(E)-Crotonaldehyde	123-73-9	3.4	3000	0.001	Forestomach lesions	PPRTV
Benzyl chloride	100-44-7	6.4	3000	0.002	Cardiotoxicity	PPRTV
Propargyl alcohol	107-19-7	5	3000	0.002	Renal and hepatotoxicity	IRIS
Acrylamide	79-06-1	0.053	30	0.002	Degenerative nerve changes	IRIS
Benzene	71-43-2	1.2	300	0.004	Decreased lymphocyte count in humans	IRIS
Epichlorohydrin	106-89-8	6.25	1000	0.006	Decreased fertility	PPRTV

Chemical	CASRN	Point of departure (mg/kg-day)	Total uncertain ty factor	RfV Chronic RfD (mg/kg-day)	Noncancer effect	Source
Dichloromethane	75-09-2	0.19	30	0.006	Hepatic effects	IRIS
Aniline	62-53-3	7	1000	0.007	Splenic effects	PPRTV
2-(Thiocyano methylthio)benzo thiazole	21564-17-0	3.8	300	0.01	Decreased body weight gain; decreased white blood cells (WBC) and plasma alanine aminotransferase (ALT)	HHBP
Furfural	98-01-1	30	3000	0.01	Liver pathology	HHBP
Naphthalene	91-20-3	71	3000	0.02	Decreased mean terminal body weight > 10%	IRIS
2-(2-Butoxyethoxy) ethanol	112-34-5	81	3000	0.03	Changes in red blood cells (RBC)	PPRTV
1,4-Dioxane	123-91-1	9.6	300	0.03	Liver and kidney toxicity	IRIS
Bisphenol A	80-05-7	50	1000	0.05	Reduced mean body weight	IRIS
1,3-Dichloropropene	542-75-6	3.4	100	0.03	Chronic irritation	IRIS
Toluene	108-88-3	238	3000	0.08	Increased absolute kidney weight	IRIS
Ethylenediamine	107-15-3	9	100	0.09	Liver and kidney toxicity	PPRTV
Ethylbenzene	100-41-4	97.1	1000	0.1	Liver and kidney toxicity; histopathology	IRIS
2-Butoxyethanol (EGBE)	111-76-2	1.4	10	0.1	Hemosiderin deposition in liver (inhalation study)	IRIS
Acetophenone	98-86-2	423	3000	0.1	General toxicity; NO LOAEL identified	IRIS
Didecyldimethyl ammonium chloride	7173-51-5	10	100	0.1	Clinical signs; decreased total cholesterol levels	HHBP

Chemical	CASRN	Point of departure (mg/kg-day)	Total uncertainty factor	RfV Chronic RfD (mg/kg-day)	Noncancer effect	Source
Cumene	98-82-8	110	1000	0.1	Increased average kidney weight in female rats	IRIS
N,N-Dimethylformamide	68-12-2	96	1000	0.1	Increase in ALT and liver weight	PPRTV
1-Butanol	71-36-3	125	1000	0.1	Hypoactivity and ataxia	IRIS
Xylenes	1330-20-7	179	1000	0.2	Decreased body weight; increased mortality	IRIS
Formaldehyde	50-00-0	15	100	0.2	Decreased weight gain	IRIS
Phenol	108-95-2	93	300	0.3	Decreased maternal weight gain; developmental toxicity	IRIS
2-Methyl-1-propanol (Isobutanol)	78-83-1	316	1000	0.3	Hypoactivity and ataxia	IRIS
Acetone	67-64-1	900	1000	0.9	Nephropathy	IRIS
Ethyl acetate	141-78-6	900	1000	0.9	Mortality and body weight loss	IRIS
Formic acid	64-18-6	277	300	0.9	Reproductive effects	PPRTV
Dodecylbenzenesulfonic acid	27176-87-0	50	100	0.5	Decreased pup weight; kidney pathology	HHBP
Ethylene glycol	107-21-1	200	100	2	Kidney toxicity; chronic nephritis	IRIS
Hexanedioic acid	124-04-9	470	300	2	Decreased body weight	PPRTV
Methanol	67-56-1	43.1 mg/L[a]	100	2	Extra cervical ribs; developmental toxicity	IRIS
Benzoic acid	65-85-0	4.4	1	4	No adverse effects observed in humans	IRIS
1,2-Propylene glycol	57-55-6	5200	300	20	Reduced red blood cell counts and hyperglycemia	PPRTV

Chemical	CASRN	Point of departure (mg/kg-day)	Total uncertainty factor	RfV Chronic RfD (mg/kg-day)	Noncancer effect	Source

[a] POD based on internal methanol blood concentration using a PBPK model.

9.5.3.2. MCDA Results: Chemical Used in Hydraulic Fracturing Fluid

The hazard potential scores of the selected 37 chemicals used in hydraulic fracturing fluid are presented in Table 9-7.

Table 9-7. MCDA results for 37 chemicals used in hydraulic fracturing fluid.

Chemicals are ranked, from high to low, based on total hazard potential score. See section 9.5.2 for details on the calculation.

Chemical	CASRN	Physicochemical properties score	Occurrence score	Toxicity score	Total hazard potential score
Propargyl alcohol	107-19-7	1.00	1.00	1.00	**3.00**
2-Butoxyethanol (EGBE)	111-76-2	1.00	1.00	0.67	**2.67**
N,N-Dimethylformamide	68-12-2	1.00	1.00	0.67	**2.67**
Acrylamide	79-06-1	1.00	0.67	1.00	**2.67**
Formaldehyde	50-00-0	1.00	1.00	0.33	**2.33**
Naphthalene	91-20-3	0.67	1.00	0.67	**2.33**
Benzyl chloride	100-44-7	0.67	0.67	1.00	**2.33**
1-Butanol	71-36-3	1.00	0.67	0.67	**2.33**
Epichlorohydrin	106-89-8	0.67	0.67	1.00	**2.33**
2-(2-Butoxyethoxy)ethanol	112-34-5	1.00	0.67	0.67	**2.33**
Methanol	67-56-1	1.00	1.00	0.00	**2.00**
Ethylene glycol	107-21-1	1.00	1.00	0.00	**2.00**
Formic acid	64-18-6	1.00	1.00	0.00	**2.00**
Didecyldimethylammonium chloride	7173-51-5	0.33	1.00	0.67	**2.00**
1,4-Dioxane	123-91-1	1.00	0.33	0.67	**2.00**
(E)-Crotonaldehyde	123-73-9	0.67	0.33	1.00	**2.00**
Aniline	62-53-3	1.00	0.00	1.00	**2.00**
Furfural	98-01-1	1.00	0.00	1.00	**2.00**

Chemical	CASRN	Physicochemical properties score	Occurrence score	Toxicity score	Total hazard potential score
1,2-Propylene glycol	57-55-6	1.00	0.67	0.00	**1.67**
Hexanedioic acid	124-04-9	1.00	0.67	0.00	**1.67**
Toluene	108-88-3	0.33	0.67	0.67	**1.67**
Phenol	108-95-2	1.00	0.33	0.33	**1.67**
2-Methyl-1-propanol (Isobutanol)	78-83-1	1.00	0.33	0.33	**1.67**
Dichloromethane	75-09-2	0.67	0.00	1.00	**1.67**
Ethylenediamine	107-15-3	1.00	0.00	0.67	**1.67**
Bisphenol A	80-05-7	1.00	0.00	0.67	**1.67**
2-(Thiocyanomethylthio) benzothiazole	21564-17-0	0.67	0.00	1.00	**1.67**
Benzene	71-43-2	0.67	0.00	1.00	**1.67**
Dodecylbenzenesulfonic acid	27176-87-0	0.33	1.00	0.00	**1.33**
Xylenes	1330-20-7	0.33	0.67	0.33	**1.33**
Ethylbenzene	100-41-4	0.33	0.33	0.67	**1.33**
Benzoic acid	65-85-0	1.00	0.33	0.00	**1.33**
Acetophenone	98-86-2	0.67	0.00	0.67	**1.33**
1,3-Dichloropropene	542-75-6	0.67	0.00	0.67	**1.33**
Cumene	98-82-8	0.00	0.33	0.67	**1.00**
Ethyl acetate	141-78-6	0.67	0.33	0.00	**1.00**
Acetone	67-64-1	0.67	0.33	0.00	**1.00**

Of the chemicals in hydraulic fracturing fluid that were considered in this hazard evaluation, propargyl alcohol received the highest overall hazard potential score. Propargyl alcohol was used in 33% of wells in the FracFocus database, making it one of the most widely used chemicals that was considered in this analysis, and it also had one of the lowest RfVs, with an RfD of 0.002 mg/kg-day. It is also hydrophilic and has relatively low volatility, indicating that it is likely to be readily transported in water. Given these properties, propargyl alcohol received the highest overall ranking across all of the metrics that were considered in the hazard evaluation.

The other chemicals that fell in the upper quartile in terms of frequency of use received lower hazard potential scores relative to propargyl alcohol, due to lower estimated toxicity and/or physicochemical properties that are less conducive to transport in water. Naphthalene, used in 19% of wells on the FracFocus database, has an RfD of 0.02 mg/kg-day, and is expected to have somewhat lower transport in water relative to other chemicals because it is moderately hydrophobic and moderately volatile. Methanol (RfD of 2 mg/kg-day), ethylene glycol (RfD of 2 mg/kg-day), 2-butoxyethanol (RfD of 0.1 mg/kg-day), formic acid (RfD of 0.9 mg/kg-day), N,N-dimethylformamide (RfD of 0.1 mg/kg-day), and formaldehyde (RfD of 0.2 mg/kg-day)—which were used in 73%, 47%, 23%, 11%, 9%, and 7% of wells in the FracFocus database, respectively—are all expected to be highly mobile in water and have low volatility, but have higher RfVs compared to many of the other chemicals in the assessment. Didecyldimethylammonium chloride (RfD of 0.1 mg/kg-day), used in 8% of wells, is expected to have reduced mobility in water due to its more hydrophobic properties.

In addition to propargyl alcohol, the other most toxic chemicals (occurring in the lowest quartile of RfVs) received moderate to high hazard potential scores overall. Acrylamide (RfD of 0.002 mg/kg-day) is used in only 1% of wells, but has physicochemical properties that are very conducive to transport in water, and therefore received one of the highest overall hazard potential scores. Benzyl chloride (RfD of 0.002 mg/kg-day) and epichlorohydrin (RfD of 0.006 mg/kg-day) are used in 6% and 1% of wells, respectively, but scored slightly lower than acrylamide with regards to their physicochemical properties. Other chemicals, including (E)-crotonaldehyde (RfD of 0.001 mg/kg-day), benzene (RfD of 0.004 mg/kg-day), dichloromethane (RfD of 0.006 mg/kg-day), aniline (RfD of 0.007 mg/kg-day), furfural (RfD of 0.01 mg/kg-day), and 2-(Thiocyanomethylthio)benzothiazole (RfD of 0.01 mg/kg-day), received lower overall scores because they are used more infrequently (each in less than 0.1% of wells in the FracFocus database).

9.5.3.3. Hazard Identification: Chemicals Detected in Flowback and Produced Water

As discussed above, a total of 23 chemicals detected in flowback and produced water were identified for hazard evaluation using the selection criteria described in Section 9.5.1. Of these 23 chemicals, 10 chemicals overlap with the hazard evaluation of chemicals used in hydraulic fracturing fluids. Because of this overlap, many of the effects noted in each hazard evaluation are similar.

These chemicals, along with their POD, total products of uncertainty factors applied, federal chronic RfVs, and the health effect bases for the RfVs, are shown in Table 9-8. As seen in Table 9-8, all of these chemicals had RfDs available from IRIS, PPRTV, or HHBP. These chemicals induce a variety of adverse outcomes, including immune system effects, changes in body weight, changes in blood chemistry, pulmonary toxicity, neurotoxicity, liver and kidney toxicity, and reproductive and developmental toxicity. The RfD values within this suite of chemicals range from 0.001−0.9 mg/kg-day, with pyridine having the lowest RfD and acetone having the highest RfD. For this subset of chemicals, 88% have an RfD within 2 orders of magnitude of each other and 78% have RfDs within a factor of 10 (range of 0.01−0.1 mg/kg-day). Some of these chemicals include chloroform, naphthalene, 1,4-dioxane, toluene, cumene, and ethylbenzene.

Although only federal RfVs are considered in this hazard evaluation, 2 of these chemicals—benzene and 1-4-dioxane—also have federal OSFs . These chemicals are also included in the hazard evaluation of chemicals used in hydraulic fracturing fluids, discussed above. 1,4-dioxane is a more potent carcinogen compared to benzene. The OSF for 1,4-dioxane is 0.1 per mg/kg-day and is classified as likely to be a human carcinogen by IRIS (U.S. EPA, 2013f).

Table 9-8. Toxicological properties of the 23 chemicals detected in flowback and produced water that were identified for hazard evaluation and MCDA analysis.

Chemicals are ranked, from low to high, based on their respective federal chronic RfVs. Chemicals in *italics* are also included in the hazard evaluation of chemicals used in hydraulic fracturing fluids.

Chemical	CASRN	Point of departure (mg/kg-day)	Total un-certainty factors	RfV	Non-cancer effect	Source
				Chronic RfD (mg/kg-day)		
Pyridine	110-86-1	1	1000	0.001	Increased liver weight	IRIS
2-Methylnaphthalene	91-57-6	3.5	1000	0.004	Pulmonary alveolar proteinosis	IRIS
Benzene	71-43-2	1.2	300	0.004	Decreased lymphocyte count in humans	IRIS
Chloroform	67-66-3	12.9	1000	0.01	Fatty cyst formation in the liver; elevated SGPT(or ALT)	IRIS
Naphthalene	91-20-3	71	3,000	0.02	Decreased mean terminal body weight > 10%	IRIS
Di(2-ethylhexyl) phthalate	117-81-7	19	1000	0.02	Increased relative liver weight	IRIS
2,4-Dimethylphenol	105-67-9	50	3000	0.02	Clinical signs; hematological changes	IRIS
Pyrene	129-00-0	75	3000	0.03	Kidney effects	IRIS
1,4-Dioxane	123-91-1	9.6	300	0.03	Liver and kidney toxicity	IRIS
Fluorene	86-73-7	125	3000	0.04	Decreased RBC, packed cell volume and hemoglobin	IRIS
Fluoranthene	206-44-0	125	3000	0.04	Nephropathy; increased liver weights; hematological alterations	IRIS
2-Methylphenol (o-Cresol)	95-48-7	50	1000	0.05	Decreased body weights and neurotoxicity	IRIS
Toluene	108-88-3	238	3000	0.08	Increased absolute kidney weight	IRIS
Carbon disulfide	75-15-0	11	100	0.1	Fetal toxicity and malformations	IRIS

Chemical	CASRN	Point of departure (mg/kg-day)	Total un-certainty factors	RfV Chronic RfD (mg/kg-day)	Non-cancer effect	Source
Cumene	98-82-8	110	1000	0.1	increased average kidney weight in female rats	IRIS
Benzyl alcohol	100-51-6	143	1000	0.1	Effects on survival, growth, and tissue histopathology	PPRTV
Dibutyl phthalate	84-74-2	125	1000	0.1	Increased mortality	IRIS
Ethylbenzene	100-41-4	97.1	1000	0.1	liver and kidney toxicity; histopathology	IRIS
Acetophenone	98-86-2	423	3000	0.1	General toxicity; no LOAEL identified	IRIS
Diphenylamine	122-39-4	10	100	0.1	Alterations in clinical chemistry; increased kidney. liver, and spleen weights	HHBP
Xylenes	1330-20-7	179	1000	0.2	Decreased body weight; increased mortality	IRIS
Phenol	108-95-2	93	300	0.3	Decreased maternal weight gain; developmental toxicity	IRIS
Acetone	67-64-1	900	1000	0.9	Nephropathy	IRIS

9.5.3.4. MCDA Results: Flowback and Produced Water

The hazard potential scores of the selected 23 chemicals detected in flowback and produced water are presented in Table 9-9.

Table 9-9. MCDA results for 23 chemicals in hydraulic fracturing flowback and produced water.

Chemicals are ranked, from high to low, based on total hazard potential score. See Section 9.5.2 for details on the calculation.

Chemical	CASRN	Physicochemical properties score	Occurrence score	Toxicity score	Total hazard potential score
Benzene	71-43-2	0.75	1.00	1.00	**2.75**
Pyridine	110-86-1	0.75	1.00	1.00	**2.75**
Naphthalene	91-20-3	0.75	0.67	1.00	**2.42**

Chemical	CASRN	Physicochemical properties score	Occurrence score	Toxicity score	Total hazard potential score
2,4-Dimethylphenol	105-67-9	1.00	0.33	1.00	**2.33**
2-Methylnaphthalene	91-57-6	0.25	1.00	1.00	**2.25**
Chloroform	67-66-3	0.75	0.33	1.00	**2.08**
2-Methylphenol	95-48-7	1.00	0.33	0.67	**2.00**
Benzyl alcohol	100-51-6	1.00	0.67	0.33	**2.00**
Bis(2-Ethylhexyl) Phthalate	117-81-7	0.25	0.67	1.00	**1.92**
Carbon Disulfide	75-15-0	0.50	1.00	0.33	**1.83**
Toluene	108-88-3	0.50	1.00	0.33	**1.83**
Acetone	67-64-1	0.75	0.67	0.00	**1.42**
Pyrene	129-00-0	0.75	0.00	0.67	**1.42**
Di-n-butyl Phthalate	84-74-2	0.75	0.33	0.33	**1.42**
1,4-Dioxane	123-91-1	1.00	0.00	0.67	**1.67**
Fluoranthene	206-44-0	1.00	0.00	0.67	**1.67**
Xylenes	1330-20-7	0.50	1.00	0.00	**1.50**
Ethylbenzene	100-41-4	0.50	0.33	0.33	**1.17**
Phenol	108-95-2	1.00	0.67	0.00	**1.67**
Diphenylamine	122-39-4	1.00	0.00	0.33	**1.33**
Isopropylbenzene	98-82-8	0.25	0.67	0.33	**1.25**
Acetophenone	98-86-2	0.75	0.00	0.33	**1.08**
Fluorene	86-73-7	0.00	0.00	0.67	**0.67**

The highest total hazard potential scores for chemicals in flowback and produced water went to benzene and pyridine, followed closely by naphthalene. These three chemicals all have RfVs that fell in the lowest (most toxic) quartile relative to other chemicals in the hazard evaluation (RfDs of 0.004, 0.001, and 0.02 mg/kg-day, respectively). Benzene fell in the upper quartile of observed chemical concentrations (with a maximum reported average concentration of 680 μg/l; Barnett shale produced water, Table E-9), while pyridine and naphthalene fell in the second highest quartile (with maximum reported average concentrations of 413 and 238 μg/l, respectively; Barnett shale produced water, Table E-10). These three chemicals only scored moderately in terms of their physicochemical properties, however, as all three are expected to have somewhat lower transport in water compared to other chemicals in the assessment. 2-Methylnaphthalene also fell in the lowest quartile in terms of toxicity (RfD of 0.004 mg/kg-day) and the highest quartile in terms of concentration (average of 1,362 μg/l; Barnett shale produced water, Table E-10), but received a slightly lower score than these chemicals with regards to physiochemical properties.

Other chemicals occurring in the upper quartile of flowback and produced water concentrations include toluene (average of 760 μg/l; Barnett shale produced water, Table E-9), xylenes (average of 360 μg/l; Barnett shale produced water, Table E-9), and carbon disulfide (median of 400 μg/l; Marcellus shale produced water, Table E-10). These chemicals all received moderate hazard potential scores, as all have higher RfDs (lower toxicity) relative to many of the other chemicals in the hazard evaluation, and are all expected to have moderate transport in water relative to the other chemicals.

Other chemicals with RfVs that fell in the lowest (most toxic) quartile in flowback and produced water include chloroform (RfD of 0.01 mg/kg-day), di(2-ethylhexyl)phthalate (RfD of 0.02 mg/kg-day), and 2,4,-dimethylphenol (RfD of 0.02 mg/kg-day). Of these, di(2-ethylhexyl)phthalate was detected at moderately high concentrations relative to other chemicals in the assessment (average of 210 μg/l; Barnett shale produced water, Table E-10), but is expected to have reduced mobility in water due primarily to its more hydrophobic properties. The rest are expected to have moderate to high transport in water, but were detected at relatively lower average concentrations compared to other chemicals in the assessment.

9.5.4. Summary of Chemicals Detected in Multiple Stages of the Hydraulic Fracturing Water Cycle

A number of chemicals with federal chronic RfVs that are used in hydraulic fracturing fluids were also found to be present in flowback and produced water stages of the hydraulic fracturing water cycle. The use of a chemical in hydraulic fracturing fluids, and subsequent presence in later stages of the hydraulic fracturing water cycle, is of particular interest in demonstrating which chemicals in this dataset may be mixed, injected, and then detected downstream in the water cycle. This section focuses on that group of chemicals.

Based on the available information in our datasets, 23 chemicals overall had federal chronic RfVs and were identified as being used in hydraulic fracturing fluids and detected in the flowback/produced water stage of the hydraulic fracturing water cycle. These chemicals are shown in Table 9-10. 10 of these chemicals were included in both the hazard evaluation of hydraulic fracturing fluids (see Table 9-6 and Table 9-7) and the flowback and produced water hazard evaluation (see Table 9-8 and Table 9-9). This means that these 10 chemicals had both frequency of use data from FracFocus and a reported measured concentration in flowback and produced water from Chapter 7 (Appendix E). These 10 chemicals included all of the BTEX chemicals, as well as naphthalene, 1,4 dioxane, acetone, acetophenone, cumene, and phenol. The chemicals of this group with the lowest chronic oral RfVs were benzene, naphthalene, and 1,4-dioxane. These chemicals all have RfDs within an order of magnitude of each other and are known or likely human carcinogens. The next chemical of this group—toluene—has an RfD 20 times greater than benzene. Overall, benzene was the most toxic of the chemicals listed in Table 9-10.

Table 9-10. List of the 23 chemicals with federal chronic RfVs identified to be used in hydraulic fracturing fluids and detected in the flowback/produced water stage of the hydraulic fracturing water cycle.

Chemical	CASRN	Used in hydraulic fracturing fluids?	FracFocus frequency of use data?	Detected in flowback or produced water?	Physicochemical properties data available?	In hazard evaluation?[a]
1,4-Dioxane	123-91-1	Y	Y	Y	Y	FF+FB
Acetone	67-64-1	Y	Y	Y	Y	FF+FB
Acetophenone	98-86-2	Y	Y	Y	Y	FF+FB
Benzene	71-43-2	Y	Y	Y	Y	FF+FB
Cumene	98-82-8	Y	Y	Y	Y	FF+FB
Ethylbenzene	100-41-4	Y	Y	Y	Y	FF+FB
Naphthalene	91-20-3	Y	Y	Y	Y	FF+FB
Phenol	108-95-2	Y	Y	Y	Y	FF+FB
Toluene	108-88-3	Y	Y	Y	Y	FF+FB
Xylenes	1330-20-7	Y	Y	Y	Y	FF+FB
1,2-Propylene glycol	57-55-6	Y	Y	Y	Y	FF
Dichloromethane	75-09-2	Y	Y	Y	Y	FF
Ethylene glycol	107-21-1	Y	Y	Y	Y	FF
Formic acid	64-18-6	Y	Y	Y	Y	FF
Methanol	67-56-1	Y	Y	Y	Y	FF
Aluminum	7429-90-5	Y	Y	Y	--	No
Iron	7439-89-6	Y	Y	Y	--	No
Di(2-ethylhexyl) phthalate	117-81-7	Y	--	Y	Y	FB
Acrolein	107-02-8	Y	--	Y	Y	No
Arsenic	7440-38-2	Y	--	Y	--	No
Chlorine	7782-50-5	Y	--	Y	--	No
Chromium (III)	16065-83-1	Y	--	Y	--	No
Chromium (VI)	18540-29-9	Y	--	Y	--	No
Zinc	7440-66-6	Y	--	Y	--	No

[a] FF+FB: chemical in both the hydraulic fracturing fluid and flowback/produced water hazard evaluations; FF or FB: chemical in either the hydraulic fracturing fluid or flowback/produced water hazard evaluations. A dash indicates data for chemical not available.

An additional 6 chemicals were included in either the hazard evaluation of hydraulic fracturing fluids (see Table 9-6 and Table 9-7) or the flowback and produced water hazard evaluation (see Table 9-8 and Table 9-9), but not both. These chemicals were reported to be have been used in hydraulic fracturing fluids and detected in flowback/produced water, but lacked the occurrence data (frequency of use or a measured concentration) to support inclusion in both of these hazard evaluations. The remaining 8 chemicals reported to have been used in hydraulic fracturing fluids or detected in flowback/produced water were not included in either of the hazard evaluations presented above because they lacked one or more of the inclusion criteria. These chemicals include acrolein as well as several metals. Arsenic and acrolein have the lowest RfDs by an order of magnitude and arsenic is classified as a known human carcinogen by the EPA, IARC, and NTP. Chromium (VI) is also classified as a known human carcinogen by IARC and NTP.

9.6. Synthesis

The overall objective of this chapter was to identify and provide information on the toxicological properties of chemicals used in hydraulic fracturing and of hydraulic fracturing wastewater constituents, and to evaluate the potential hazard of these chemicals to drinking water resources. Toward this end, the EPA developed a comprehensive list of 1,173 chemicals with reported occurrence in the hydraulic fracturing water cycle, separating them into subsets based on whether they were reported to have been used in hydraulic fracturing fluids or detected in flowback and produced water. First, for each of these chemicals, RfVs and OSFs from selected federal, state, and international sources were collected when available. Second, for subsets of chemicals that were identified as being of interest in previous chapters of this report, federal chronic RfVs were used to conduct an initial identification of the potential human health hazards inherent to these chemicals. Finally, for other subsets of chemicals that had data available, an approach for a more data-informed hazard evaluation was illustrated by integrating data on federal chronic RfVs, occurrence, and physicochemical properties using an MCDA framework.

9.6.1. Summary of Findings

Across the industrial landscape, thousands of chemicals are used commercially that lack toxicity data (Judson et al., 2009). Similarly, major knowledge gaps exist regarding the toxicity of most chemicals used in hydraulic fracturing fluids or detected in flowback/produced water, impeding the assessment of human health risks associated with drinking water resources affected by hydraulic fracturing.

Of the 1,076 chemicals used in hydraulic fracturing fluids, chronic RfVs and/or OSFs from all of the selected federal, state, or international sources were available for 90 chemicals (8.4%). From the federal sources alone, chronic oral RfVs were available for 73 chemicals (6.8%), and OSFs were available for 15 (1.4%). Potential hazards associated with these chemicals include carcinogenesis, immune system effects, changes in body weight, changes in blood chemistry, cardiotoxicity, neurotoxicity, liver and kidney toxicity, and reproductive and developmental toxicity.

Of the 134 chemicals that are reported to have been detected in hydraulic fracturing flowback or produced water, chronic RfVs and/or OSFs from all of the selected federal, state, or international sources were available for 83 chemicals (62%). From the federal sources alone, chronic RfVs were available for 70 chemicals (52%), and OSFs were available for 20 (15%). Potential hazards associated with these chemicals include carcinogenesis, immune system effects, changes in body weight, changes in blood chemistry, pulmonary toxicity, neurotoxicity, liver and kidney toxicity, and reproductive and developmental toxicity.

Of the chemicals included in the hazard evaluations, benzene is the only one of these chemicals with an OSF that is classified as a known human carcinogen, while acrylamide was found to be the most potent likely human carcinogen. Several other chemicals, including 1,4-dioxane, dichloromethane, naphthalene, and ethylbenzene are also classified as possible, probable, or likely human carcinogens.

Toxicity information spans a wide range with respect to extent, quality and reliability. The sources of RfVs and OSFs selected for the purposes of this chapter are based on criteria developed specifically for this report. For the total 1,173 chemicals identified on the EPA's list, federal, state, and international chronic RfVs and/or OSFs that met stringent selection criteria were available for 147 (13%) of the chemicals. Several of the RfVs from selected sources were derived using UFs of up to several orders of magnitude, indicating uncertainty when comparing chemicals for potential toxicity and identifying the chemicals that may be more likely to present a human health hazard. For many of the chemicals used in hydraulic fracturing or found in flowback or produced water there may be relevant information, including cancer and noncancer-related information, from one or more sources that were not evaluated in this chapter. In instances where toxicity data is not available from selected sources, risk assessors may need to draw from alternative sources of hazard information. The chapter discusses two available resources for consideration when RfVs and/or OSFs are not available: QSAR-predicted toxicity data, and toxicity data from the EPA's ACToR database. Oral toxicity data was available on ACToR for 642 (55%) of the chemicals. The information available in the ACToR data warehouse ranges from the federal RfVs discussed in Section 9.3.1, which have undergone extensive peer review, to RfVs and study and test results that have undergone little to no peer review.

When considering the potential impact of chemicals on drinking water resources and human health, it is important to consider exposure as well as toxicological properties. The majority of chemicals identified in this report lacked the necessary data to conduct such an assessment. However, integrating data on toxicity, occurrence, and physicochemical properties using an MCDA framework enabled a more data-informed hazard evaluation on some chemicals. This analysis highlighted several chemicals that may be more likely than others to reach drinking water and create a toxicological hazard. In hydraulic fracturing fluid, an example is propargyl alcohol. It was among the chemicals with the lowest RfVs considered in this hazard evaluation, was used in 33% of wells in the FracFocus database, and is water soluble with low volatility. In flowback and produced water, examples of such chemicals include benzene, pyridine, and naphthalene. These chemicals were also among those with the lowest RfVs considered in this hazard evaluation, are expected to be relatively mobile in water, and were present at relatively high average concentrations in flowback.

9.6.2. Factors Affecting the Frequency or Severity of Impacts

When assessing chemical hazards, there are multiple pieces of information that could be taken into account. This includes knowledge of the chemicals used at a given well site, the toxicological and physicochemical properties of these chemicals, the amount of fluid being used and recovered, the likelihood of well integrity failures, and the likelihood of spills and other unintentional releases. These topics were previously discussed in Chapters 5 through 8 of this report. Because of the large volumes of fluid being injected, even chemicals representing a small percentage of the total fluid by mass may pose a potential for exposure in the event of a spill or leak.

Overall, contamination of drinking water resources depends on site-, chemical-, and fluid-specific factors (Goldstein et al., 2014), and the exact mixture and concentrations of chemicals at a site will depend upon the geology and the company's preferences. Therefore, potential hazard and risk considerations are best made on a site-specific, well-specific basis. While the MCDA results in this chapter illustrate an approach to evaluate the relative hazards of these chemicals at the national level, a site-specific hazard evaluation would be necessary in order to identify chemicals of concern at the local level.

For example, consider (E)-crotonaldehyde, which is one of the more toxic chemicals considered in the hazard evaluation of hydraulic fracturing fluids. (E)-crotonaldehyde is reportedly used in only 0.06% of wells in the FracFocus database, based on the EPA's analysis. If the FracFocus database represents a fair sample of all of the wells across the country, then the likelihood of (E)-crotonaldehyde contamination on a nationwide scale is limited. However, this in no way diminishes the likelihood of (E)-crotonaldehyde contamination at well sites where this chemical is used. Therefore, potential exposures to more toxic but infrequently used chemicals are more of a local issue, rather than a national one.

This is in contrast with methanol, which was reported in 73% of wells in the FracFocus database. Methanol is soluble and relatively mobile in water, but has a higher RfV relative to other chemicals in the hazard evaluation. Therefore, when considering chemical usage on a nationwide basis, methanol may be expected to have a higher exposure potential compared to other chemicals, with a moderate overall hazard potential due to its relatively high RfV.

9.6.3. Uncertainties

There are several notable uncertainties in the chemical and toxicological data that limit a comprehensive assessment of the potential health impacts of hydraulic fracturing on drinking water resources.

For the purposes of this chapter, the lack of RfVs and OSFs from the sources meeting stringent selection criteria is the most significant data gap. For instance, of the 32 chemicals (excluding water, quartz, and sodium chloride) that are used in ≥10% of wells nationwide according to FracFocus, federal chronic RfVs were only available for 7 chemicals. Without these reliable and peer reviewed data, comprehensive hazard evaluation and hazard identification of chemicals is difficult, and the ability to consider the potential cumulative effects of exposure to chemical mixtures in hydraulic fracturing fluid, flowback, or produced water is limited. Consequently, potential impacts on drinking water resources and human health may not be assessed adequately.

Another major uncertainty lies in the total list of chemicals that was compiled for this chapter. As discussed in Section 5.1.3, information is lacking on the chemicals that are used in hydraulic fracturing fluid formulation. CBI chemicals, which were present in approximately 70% of well records on the FracFocus database, were excluded from the EPA's analysis. The analysis also excluded ingredient records that were not able to be assigned standardized chemical names, which resulted in approximately 35% of FracFocus ingredient records being excluded from the report. This lack of data limits the ability to more completely assess the impact of chemicals that are potentially used with great frequency. Moreover, there may be a regional bias in the EPA's analysis of FracFocus, as 78% of chemical disclosures in the FracFocus database came from five states, and 47% were from Texas. Despite these limitations, the FracFocus database remains the most complete source for tracking hydraulic fracturing chemical usage in the United States, and therefore was the best available source for the hazard evaluation in this chapter. Although the sources used to compile the chemical list represented the best available data at the time of this study, it is possible that some of these chemicals are no longer used at all, and many of these chemicals may only be used infrequently. Therefore, it may be possible that significantly fewer than 1,076 chemicals are currently used in abundance. Consequently, having a better understanding of the chemicals and formulations, including those that are CBI, along with their frequency of use and volumes, would greatly benefit risk assessment and risk management decisions.

Additionally, the list of flowback and produced water chemicals identified in this chapter is almost certainly incomplete. Few studies to date have examined the chemical composition of flowback and produced water, and the hazard evaluation in this chapter relied on data from the relatively small number of studies that are presented in Appendix E of this assessment. As discussed in Chapter 7, chemicals and their metabolites may go undetected simply because they were not included in the analytical methodology. Additionally, chemical analysis of flowback and produced water may be challenging, because high levels of dissolved solids in flowback and wastewater can interfere with chemical detection. As a result, it is likely that there are chemicals of concern in flowback and produced water that have not been detected or reported.

Finally, when considering the MCDA framework that was used to illustrate an approach for hazard evaluation, it should be noted that the physicochemical variables were chosen specifically to reflect chemical mobility and persistence in water. While this framework draws attention towards those chemicals that are most likely to be carried in water, it does not attempt to address the numerous other physicochemical variables that may affect chemical exposure. For instance, as discussed in Chapter 5, hydrophobic chemicals may act as long-term sources of pollution by sorbing to soils or sediments. Additionally, volatile chemicals that dissipate into the air have the potential to pose air pollution hazards, which are not considered in this drinking water assessment; or could potentially be deposited in bodies of water that are distant from the hydraulic fracturing site. Furthermore, as discussed in Chapter 5, chemical fate and transport will be influenced by environmental and site-specific conditions. The fate of a chemical in a chemical mixture will be also influenced by the other chemicals that are present in the mixture, and the relative concentrations of each. Although the assessment of these various scenarios is outside the scope of this report, the potential hazards associated with hydrophobic or volatile chemicals should not be discounted when interpreting the results of this hazard evaluation. It should be emphasized that the MCDA framework illustrated in this chapter represents just one method that can be used to integrate chemical data for hazard evaluation, and is readily adaptable to include different variables, different weights for the variables, and site-specific considerations.

9.6.4. Conclusions

The EPA has identified 1,173 chemicals used or detected in the hydraulic fracturing water cycle. Toxicity-based chronic RfVs and/or OSFs from sources meeting selection criteria are not available for the large majority (87%) of these chemicals. In addition, 56% of these chemicals do not have physicochemical property data. Furthermore, 36% of the chemicals used in hydraulic fracturing fluids lack data on their nationwide frequency of use, and very few studies have analyzed the chemical composition of flowback and produced water. Given the large number of chemicals used or detected in various stages of the hydraulic fracturing water cycle, as well as the large number of hydraulic fracturing wells nationwide, this missing chemical information represents a significant data gap. Because of these large data gaps for drinking water resources, it remains challenging to fully understand the toxicity and potential health impacts for single chemicals as well as mixtures of chemicals associated with hydraulic fracturing processes. This chapter provides an initial overall assessment of the potential human health effects associated with hydraulic fracturing on a nationwide basis. It also provides tools that may support risk assessment and risk management decision making at the local and regional level.

The toxicological data, occurrence data, and physicochemical data compiled in this report provide a resource for assessing the potential hazards associated with chemicals in the hydraulic fracturing water cycle. Additionally, the MCDA framework presented herein illustrates one method for integrating these data for hazard evaluation. While the analysis in this chapter is constrained to the assessment of chemicals on a nationwide scale, this approach is readily adaptable for use on a regional or site-specific basis.

This collection of data provides a tool to inform decisions about protection of drinking water resources. Agencies may use these results to prioritize chemicals for hazard assessment or for determining future research priorities. Industry may use this information to prioritize chemicals for replacement with less toxic, persistent, and mobile alternatives. A summary of the findings related to the overall objective of this chapter and the research questions is presented in Text Box 9-1.

Text Box 9-1. Research Questions Revisited.

What are the toxicological properties of hydraulic fracturing fluid chemical additives?

- In a nationwide assessment, the EPA identified 1,076 chemicals that are used in hydraulic fracturing fluids. This does not include chemicals classified as CBI, which the FracFocus database indicates are used in more than 70% of wells. Chronic RfVs and/or OSFs from selected federal, state, and international sources were available for 90 (8.4%) of these chemicals. From the federal sources alone, chronic RfVs were available for 73 chemicals (6.8%), and OSFs were available for 15 chemicals (1.4%). RfVs and OSFs were not available for the majority of chemicals that are used in hydraulic fracturing fluid, representing a significant data gap with regards to hazard identification. Of the chemicals that have selected RfVs, health effects include the potential for carcinogenesis, immune system effects, changes in body weight, changes in blood chemistry, cardiotoxicity, neurotoxicity, liver and kidney toxicity, and reproductive and developmental toxicity.
- When considering the hazard evaluation of these chemicals on a nationwide scale, chemicals such as propargyl alcohol stand out for their relatively lower RfVs, high frequency of use, and expected transport and mobility in water. However, the FracFocus database indicates that most chemicals are used infrequently on a nationwide scale; therefore, potential exposures to the majority of these chemicals are more likely to be a local issue, rather than a national one. Accordingly, potential hazard and risk considerations for hydraulic fracturing fluid chemical additives are best made on a site-specific, well-specific basis.

What are the toxicological properties of hydraulic fracturing wastewater constituents?

- This assessment identified 134 chemicals that are reported to have been detected in hydraulic fracturing flowback or produced water. These include chemicals that are added to hydraulic fracturing fluids during the chemical mixing stage, as well as naturally occurring organic chemicals, metals, naturally occurring radioactive material, and other subterranean chemicals that may be mobilized by the hydraulic fracturing process. Chronic RfVs and/or OSFs from selected federal, state, and international sources were available for 83 (62%) of these chemicals. From the federal sources alone, chronic RfVs were available for 70 chemicals (52%), and OSFs were available for 20 chemicals (15%). Of the chemicals that had selected RfVs, health effects include the potential for carcinogenesis, immune system effects, changes in body weight, changes in blood chemistry, pulmonary toxicity, neurotoxicity, liver and kidney toxicity, and reproductive and developmental toxicity.
- In a hazard evaluation of flowback and produced water data, chemicals such as benzene, pyridine, and naphthalene stood out for their relatively lower RfVs, high average concentrations, and expected transport and mobility in water. However, the chemicals present in flowback and produced water are likely to vary on a regional and well-specific basis as a result of geological differences as well as differences between hydraulic fracturing fluid formulations. Therefore, potential hazard and risk considerations are best made on a site-specific basis.

9.7. References for Chapter 9

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9.8. Annex

9.8.1. Calculation of Physicochemical Property Scores (MCDA Hazard Evaluation)

Section 9.5.2 describes how physicochemical properties scores were based on three subcriteria: mobility, volatility, and persistence. These subcriteria scores were calculated as follows:

Mobility score: Chemical mobility in water was assessed based upon three physicochemical properties: the octanol-water partition coefficient (K_{ow}), the organic carbon-water partition coefficient (K_{oc}), and aqueous solubility. K_{ow} and aqueous solubility were previously discussed in Section 5.8.3. K_{oc} is a partitioning coefficient that measures the amount of chemical that is adsorbed onto soil organic carbon per the amount of chemical that is dissolved in water. Like K_{ow}, K_{oc} is typically reported as a base-10 logarithm (log K_{oc}). From EPI Suite™, K_{oc} was estimated using the MCl Method. Chemicals with low K_{ow} and K_{oc} values are hydrophilic, and thus are more likely to move with water rather than sorbing to soils or sediments. Chemicals with high aqueous solubility are also more likely to move with water. Therefore, chemicals with low K_{ow}, low K_{oc}, or high aqueous solubility were ranked as having greater potential to affect drinking water resources. Using the thresholds designated in Table 9-5, each of these properties was assigned a score of 1-4. The highest of these three scores was designated as the mobility score for each chemical.

Volatility score: Chemical volatility was assessed based on the Henry's law constant, which was previously discussed in Section 5.8.3. Chemicals with low Henry's law constants are less likely to leave water via volatilization, and were therefore ranked as having greater potential to impact drinking water. Using the thresholds designated in Table 9-5, the Henry's law constant for each chemical was assigned a score of 1-4. This value was designated as the volatility score for each chemical.

Persistence score: Chemical persistence was assessed based on estimated half-life in water, which describes how long a chemical will persist in water before it is transformed or degraded. From EPI Suite™, half-life in water was estimated using the Level III Fugacity model. Chemicals with longer half-lives are more persistent, and were therefore ranked as having greater potential to affect drinking water. Using the thresholds designated in Table 9-5, the half-life of each chemical was assigned a score of 1-4. This value was designated as the persistence score for each chemical.

For each chemical, the mobility score, volatility score, and persistence score (each on a scale of 1 to 4) were summed to calculate a total physicochemical score. The total scores were then standardized by scaling to the highest and lowest scores observed in the subset of chemicals, using the equation described in Section 9.5.2.4.

9.8.2. Example of MCDA Score Calculation

For an example of how the MCDA scores were calculated, consider benzene. This demonstrates how the MCDA score was calculated for benzene in the hazard evaluation of chemicals used in hydraulic fracturing fluids:

- With regards to toxicity (Appendix G), benzene was found to have a federal RfD of 0.004 mg/kg-day (source: IRIS). Within the entire set of chemicals in this hazard evaluation, federal RfDs ranged from 0.001 mg/kg-day [(E)-crotonaldehyde] to 20 mg/kg-day (1,2-propylene glycol). The RfD of benzene fell in the lowest (most toxic) quartile of these scores, and therefore was given a toxicity score of 4. When the results were standardized to the highest score (4) and lowest score (1) within the set of chemicals, benzene was calculated to have a toxicity score of 1, as follows:

$$1 = (4 - 1) / (4 - 1)$$

- Benzene was used in 0.0056% of wells nationwide (U.S. EPA, 2015a). This usage frequency falls in the lowest quartile of chemicals, and therefore benzene was given an occurrence score of 1. When the results were standardized to the highest score (4) and lowest score (1) within the set of chemicals, benzene was calculated to have an occurrence score of 0, as follows:

$$0 = (1 - 1) / (4 - 1)$$

- Based on physicochemical properties, benzene received a mobility score of 4 (log K_{ow} = 2.13; log K_{oc} = 1.75; solubility = 2000 mg/l), a volatility score of 2 (Henry's law constant = 0.00555), and a persistence score of 2 (half-life in water = 37.5 days). These scores sum to a total physicochemical properties score of 8. Within the entire set of chemicals in this hazard evaluation, several chemicals received total scores of 9, which was the highest observed score. Cumene received a total score of 6, which was the lowest observed score. When the results were standardized to the high score (9) and low score (6) using the equation above, benzene was calculated to have a physicochemical properties score of 0.67 as follows:

$$0.67 = (8 - 6) / (9 - 6)$$

To calculate the total hazard potential score for benzene, the physicochemical properties score, toxicity score, and occurrence score were summed for a total of 1.67. These results can be seen in Table 9-7, which shows the MCDA results for chemicals used in hydraulic fracturing fluid.